HYDROGEN PEROXIDE in ORGANIC CHEMISTRY

John G. Wallace

E. I. du Pont de Nemours & Co. (Inc.)

BETTER THINGS FOR BETTER LIVING . . . *THROUGH CHEMISTRY*

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First printing May 1960
Second printing September 1960
Third printing, index added, September 1962

Library of Congress Catalog Card Number: 62-21025

QD
281
.W34

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FOREWORD

The Du Pont Company, producer of "Albone"* hydrogen peroxide, has compiled a general review of the literature on the use of hydrogen peroxide in organic oxidations. This review is designed primarily to assist the chemical industry in the development of new organic chemicals through the use of hydrogen peroxide.

The reactions of hydrogen peroxide are presented here on the basis of the optimum reaction conditions ordinarily required to carry out specific reactions. In this way the reader will have an immediate conception of the reaction conditions on which to base a proposed process. However, the Du Pont Company makes no guarantee of results and assumes no obligation or liability in this connection.

It is emphasized that many procedures mentioned in this text are covered by patents. Before adopting any of these procedures or processes, the manufacturer should ascertain whether or not licenses are available and arrange to obtain the necessary licenses.

An effort has been made in this publication to group a large number of patent references by subject matter. No attempt has been made to define these patent references in terms of the various claims which they cover. In all cases, these references are cited strictly from a technical standpoint. No representation is made that all patents of interest are cited.

Special attention is directed to the hazards and safety precautions described in the section on safety, page 114.

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INTRODUCTION

Hydrogen peroxide is today reaching a significant stage in its development as an oxidizing agent for organic compounds. Largely responsible for the new emphasis on hydrogen peroxide has been the epoxidation reaction. The use of hydrogen peroxide in epoxidation for the manufacture of plasticizers and insecticides has shown a very rapid growth – so rapid, in fact, that sales of hydrogen peroxide for chemical uses now amount to a considerable part of all peroxide sales. Consumption of hydrogen peroxide in organic oxidations, judging from recent trends, may easily be doubled in the next decade.

Many of the organic reactions of hydrogen peroxide have been known for many years, yet commercial application of these reactions has been realized only recently. A simple explanation for their belated commercialization appears to be the relatively high cost for hydrogen peroxide. The cost aspect, however, may be improved considerably by the development of new, efficient processes for the use of hydrogen peroxide. For example, hydrogen peroxide is being used in epoxidation under conditions allowing the use of a one-stage reaction with virtual elimination of solvents and corrosive catalysts (102, 350). The importance of efficient operations in reducing costs has been proved in the development of peroxide bleaching systems for cottons. Today peroxide bleaching systems have world-wide acceptance because of high production capacity, low operating costs, and high quality of the product (28). Many once considered bleaching cotton with hydrogen peroxide impractical.

Another factor affecting economics is that hydrogen peroxide has a very low equivalent weight tending to compensate for its relatively high cost. This factor can be used to economic advantage in oxidizing compounds of relatively high molecular weight.

Hydrogen peroxide in the solutions supplied commercially is very stable with respect to maintaining its active oxygen (412). This was not always true – another factor which delayed its use in chemical reactions. In earlier days, refluxing a 35% hydrogen peroxide solution for one hour was likely to result in considerable active oxygen loss. Today this same concentration can be refluxed for 10 - 15

hours with almost no active oxygen loss. The increased stability of hydrogen peroxide has been the result of improved methods of stabilization, shipping, and storage. Its excellent stability, however, does not necessarily extend into situations where contamination by such extraneous matter as heavy metal salts has occurred.

The efficiency of reactions employing hydrogen peroxide may be dependent upon the absence of deleterious contaminants, the careful preparation of reactor surfaces, and the use of proper materials of construction. Where these factors are disregarded, wasteful decomposition of hydrogen peroxide may occur. Evolution of oxygen gas from a hydrogen peroxide system, or a hydrogen peroxide-derived system, usually indicates decomposition. Undesirable decomposition may be diminished by use of properly cleaned glassware or carefully passivated stainless steel (type 18-8) equipment. In general, hydrogen peroxide decomposes rapidly in iron or mild steel equipment under reaction conditions.

Comparison of Oxidizing Agents

The oxidizing action of hydrogen peroxide is due entirely to the presence of a peroxidic oxygen atom in the molecule. This oxygen atom is termed active oxygen and is measured by titration with a number of reagents (189, 210, 380). Once peroxidic oxygen is converted to molecular oxygen, the characteristic reactions of the active oxygen can no longer be expected. The reactions of hydrogen peroxide, and therefore of its active oxygen, are separate and distinct from those of the classical inorganic oxidizing agents. Sometimes the same end products are obtained, but different mechanisms may be involved.

The great difficulty with the inorganic oxidizing agents lies in obtaining a product free of contamination by byproducts and by the reduced state of the oxidizing agent itself. The reduced state of hydrogen peroxide is water. The advantage of hydrogen peroxide in this respect is apparent from the following table:

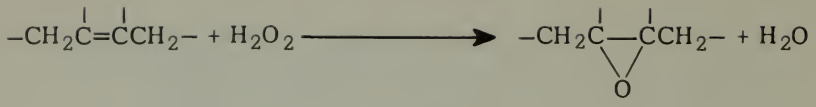
Oxidizing Agent	Reduced State
H_2O_2	H_2O
$KMnO_4$	MnO_2
NaOCl	NaCl
HIO_4	HIO_3
HIO_3	HI, I_2
Ag_2O	Ag
CuO	Cu_2O
SeO_2	Se
$AgI(OCOC_6H_5)_2$	AgI
$Pb(OCOCH_3)_4$	$Pb(OCOCH_3)_2$
$K_2Cr_2O_7$	Cr_2O_3
CrO_3	Cr_2O_3
PbO_2	PbO
OsO_4	OsO_3

Choice of an efficient oxidizing agent, of course, is governed mainly by whether or not the desired product is obtained in a sufficient state of purity. Products with a high degree of purity are easily obtained with hydrogen peroxide.

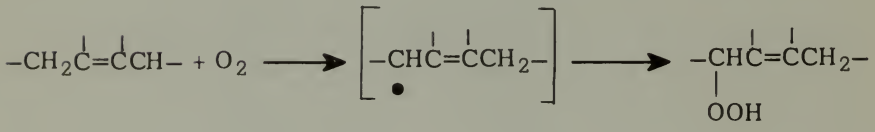
Oxidations with hydrogen peroxide systems also tend to be specific. By use of peroxide, one can often avoid the complex mixtures of oxidation products likely to be obtained with such agents as nitric acid or air.

A few reactions (17) depend upon the decomposition of hydrogen peroxide to provide molecular oxygen. Such is the case with the glucose-oxidase-catalase system (425) for desugaring eggs by oxidizing glucose to gluconic acid prior to drying. These reactions are not classified with those involving the peroxidic or active oxygen function.

Hydrogen peroxide and air, or oxygen, are sometimes considered to be interchangeable. This is a misconception resulting from the fact that the same end products are obtained in a few instances. In these cases, air oxidation probably produces an intermediate peroxidic function. The difference between air and hydrogen peroxide is illustrated in their reactions with olefins. Hydrogen peroxide under appropriate conditions produces epoxides.



The auto-oxidation of an olefin is believed to produce an intermediate stable allylic free radical which favors oxidative attack at the carbon atom alpha to the double bond. Thus a hydroperoxide is formed.



The hydroperoxides may then be converted into ketones and alcohols. Small amounts of epoxides found in these auto-oxidation mixtures seem to indicate that the double bond is being attacked by oxygen. It is possible, however, that the hydroperoxide formed is epoxidizing the olefin at a slow rate.

There are four reaction conditions ("activated states") under which hydrogen peroxide finds general and efficient use. These are (a) as organic and inorganic peracids, (b) in aqueous and alcoholic alkaline systems, (c) in neutral systems, and (d) under activation by metal salts or oxides. There are other means (333) of activating hydrogen peroxide, but these have not found wide use as yet. In general, the reaction is faster and the yields greater if hydrogen peroxide is used as an organic peracid either preformed or prepared *in situ*. By the *in situ* formation of peracid is meant a one-step reaction in which peracid is formed and used in the presence of the material to be oxidized.

THE PERACID SYSTEMS

In strong aliphatic acid solutions, hydrogen peroxide exists in equilibrium with the corresponding organic peracid.

$$RC(=O)-OH + H_2O_2 \rightleftharpoons RC(=O)-OOH + H_2O$$

In the absence of such strong acid catalysts as mineral acids, the attainment of equilibrium is impractically slow, especially at temperatures below 40°C. At higher temperatures, it is difficult to prevent the excessive loss of active oxygen unless the oxidizable organic substance is also present to react with the peracid as it forms. For this reason, it is common practice, wherever possible, to employ hydrogen peroxide under conditions for the *in situ* formation of the organic peracid at temperatures ranging up to the boiling point of the aliphatic acid.

Of the organic peracid systems, mixtures of hydrogen peroxide and glacial acetic acid or formic acid are the most used in organic syntheses. Acetic anhydride is occasionally employed (128, 140, 202, 297, 372) in the peracetic acid system to hasten the equilibrium formation of peracid. However, the use of acetic anhydride adds to the hazards of the reaction by increasing its exothermic nature and by allowing the byproduct formation of explosive diacetyl peroxide. Mixtures of formic acid and hydrogen peroxide do not require the use of a strong acid catalyst to hasten the equilibrium formation of performic acid. Hence this system used under conditions for the *in situ* formation of performic acid is an efficient one. Less stable to decomposition than peracetic acid, performic acid solutions have increased stability if prepared with specially distilled "peracid-grade" formic acid now commercially available (207).

Other organic peracid-hydrogen peroxide systems occasionally mentioned include the perpropionic (246), perbutyric (194), monoperphthalic (60,378), and trifluoroperacetic (155) acid systems. Perbenzoic acid is prepared by other means; for example, by treating (195) benzoyl chloride with aqueous sodium peroxide. An excellent review of the preparation and properties of the organic peracids has been given by Swern (437).

Trifluoroperacetic acid ($F_3C\text{-}CO_3H$) has been investigated by Emmons and co-workers (155, 156, 157, 159). Because of the exceptional acidity of trifluoroacetic acid, equilibrium concentrations of trifluoroperacetic are formed rapidly in mixing trifluoroacetic anhydride or excess trifluoroacetic acid and hydrogen peroxide. Little is known of the potential hazards of this peracid and care should be exercised in its use until the hazards, if any, have been clarified.

Comparison of the hydrogen peroxide-peracid systems with other oxidizing agents has been made by Waters (474). The peracids, in general, are applicable over a wider range of reaction conditions. They can be used in non-ionizing solvents such as chloroform or benzene as well as in solutions of organic acids. An inorganic peracid, Caro's acid or monopersulfuric acid, is occasionally used with good results in organic oxidations. It can be prepared (497) in the manner of the organic peracids by mixing hydrogen peroxide carefully with cold concentrated sulfuric acid.

$$H_2SO_4 + H_2O_2 \rightleftharpoons HSO_3\text{-}OOH + H_2O$$

Caro's acid can also be prepared by dissolving potassium persulfate ($K_2S_2O_8$) in strong sulfuric acid. Such solutions then become much more powerful oxidizing agents than aqueous persulfate solutions just as the oxidizing power of hydrogen peroxide is increased by dissolution in an organic acid (or sulfuric acid).

For reasons which are discussed more fully in the section on hazards, the use of hydrogen peroxide concentrations greater than 50% in the preparation of peracids should be avoided where lower concentrations are suitable.

Epoxidation

The reaction of an organic peracid with an olefinic material leads to an epoxy (oxirane) compound (147, 437) as a primary product.

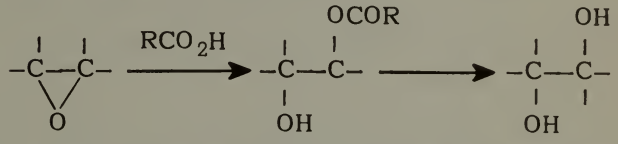
$$-\overset{|}{C}=\overset{|}{C}- + RCO_3H \longrightarrow -\overset{|}{C}-\overset{|}{C}- + RCO_2H$$

(the C–C bond is part of an epoxide ring, O)

The reaction as depicted, however, is two stage since peracid must be preformed in a preliminary stage.

$$RCOOH + H_2O_2 \overset{H+}{\rightleftharpoons} RCO_3H + H_2O$$

Under the influence of strong acid catalysts and vigorous reaction conditions, epoxides are cleaved by the organic acids present to form hydroxyacyloxy derivatives. These hydroxyacyloxy compounds are easily saponified to glycols.



Prior to about 1949, the epoxidation reaction was used (97) mainly as a laboratory tool. The discovery of methods to eliminate side reactions and to conduct epoxidation without resorting to the prior formation of peracid has given commercial scope to epoxidation. The chemical industry has found the epoxidation reaction useful for the production of insecticides, drugs and cosmetics, and plasticizer-stabilizers for such resins as polyvinyl chloride. The large number of reactions which epoxides undergo (147) also give promise of valuable chemical intermediates by epoxidation.

A large number of potential uses (147) for epoxides are disclosed in the literature. Such uses include synthetic drying compositions, coatings, adhesives, paint and varnish compositions, waxes, and lubricants. Many chemicals react with the epoxy ring to produce glycols, chlorohydrins, hydroxy-acyloxy derivatives, amino alcohols, and hydroxy nitriles and mercaptans. Certain epoxides are readily polymerized to give candidates for softening and thickening agents. Epoxides, therefore, are considered exceptionally valuable chemicals.

Practically all peracids have been investigated at one time or another as epoxidizing agents. Perbenzoic acid in an inert solvent was first used (373) in 1909. Since then performic acid, prepared (350) *in situ* with a minimum of formic acid, and peracetic acid in glacial acetic acid (448) have been used to epoxidize such unsaturated fatty glycerides as soybean oil. Perbenzoic acid is an expensive

reagent, and the separation of the reduced state, benzoic acid, is often difficult. Therefore, epoxy derivatives are prepared commercially with the other two peracid reagents.

Perbenzoic acid, readily prepared by the autoxidation of benzaldehyde, has been used to prepare a large number of epoxy compounds (36, 90, 361, 373, 441, 442, 473, 482). Monoperphthalic acid has also been employed to convert unsaturated compounds to the corresponding epoxides (89, 437). Although good yields of epoxide are usually obtained with either peracid, the necessity of using anhydrous and inert solvents has limited commercial interest in these peracids.

Although not as commercially attractive as the common peracids, perbenzoic and monoperphthalic acids often give fewer byproducts in epoxidation. Therefore, these peracids are sometimes used to prepare experimental quantities of unknown epoxides. Monoperphthalic acid (378) is conveniently prepared in the laboratory by simply dissolving phthalic anhydride in 35% hydrogen peroxide.. After a short reaction period at 45°-65°C., the peracid is crystallized by cooling.

The trifluoroperacetic acid system of Emmons (157) is also a likely laboratory reagent for epoxidation. The use of sodium carbonate or bicarbonate buffers to neutralize the acidity of the fluorinated acid in the system provides an effective means of epoxidizing certain non-fats which produce epoxides sensitive to cleavage by acids. The fluorinated peracid apparently exerts less acidity than either performic or peracetic acid to catalyze (407) epoxy cleavage. Although terminally bonded olefins are epoxidized readily by buffered trifluoroperacetic acid, the epoxidation of negatively substituted olefins is not satisfactory.

Early work indicated that peracetic acid could not be used for epoxidation of olefinic compounds since the products isolated were glycols or hydroxyacetates. Arbusow and Michailow (6) and others (52), however, found that oxidation of α-pinene with peracetic acid in ether solution gave an 89% yield of epoxide, whereas peracetic acid in acetic acid solution gave only the hydroxyacetate. Subsequent investigators (167, 389, 440) found that with relatively short reaction periods and low temperatures,

peracetic acid in acetic acid could be used for epoxidation of unsaturated substances.

Epoxidation of non-fats generally requires the use of peracid in an inert solvent such as chloroform or benzene although a few substances have been successfully epoxidized with peracid in glacial organic acid as solvent (117,372,438). A difficulty in non-fat epoxidation using hydrogen peroxide in acetic acid has been the tendency of formation of large proportions of the hydroxyacetate derivative through cleavage of the epoxy ring by the acetic acid solvent. A great percentage of the olefin sometimes remains unreacted also (440). That little epoxidation is obtained in such cases is not surprising since certain epoxy compounds (167), when dissolved in an excess of glacial acetic acid, are converted completely to hydroxyacetates in one hour at 100°C. and in four hours at 65°C. The rate of conversion is only 1% per hour at 25°C. Sulfuric acid, often used as a catalyst in preforming peracetic acid, also acts to open the epoxy ring. Peracetic acid solutions containing sulfuric acid, therefore, are not generally useful in epoxidation until the sulfuric acid has been neutralized. Cyclooctene (117), however, produced good yields (69%) of epoxide in the presence of sulfuric acid catalyst. Furan derivatives treated (57) with peracetic acid in acetic acid containing traces of mineral acid generally formed polymerized, isomerized, or cleavage products.

The ease of epoxidation depends to an extent upon the structure of the unsaturated substance. Epoxidation of isolated double bonds, such as are present in most fatty acids and oils, occurs easily in 2-4 hours. Such terminally unsaturated compounds as 1-octadecene and 1-tetradecene, on the other hand, require (439) 28 hours for substantial reaction. A study (436) of the reaction rates of peracids on olefins shows that substitution of alkyl groups for the hydrogen atoms attached to the double bond increases the rate. Also, in compounds like isoprene, the more substituted double bond is attacked first, in spite of the greater steric hindrance. The rate is decreased when such electron-attracting groups as carbonyl or carboxyl groups (48, 491) are attached to, or are in close proximity to, the double bond.

In the epoxidation of compounds containing conjugated double bonds, reaction proceeds at a much slower rate after 50% epoxidation has been effected (420). Thus, peracids can be used as analytical agents to differentiate between isolated and conjugated double bond systems (420).

Such substances as α,β-unsaturated ketones and 1,4-naphthoquinones are not readily epoxidized by peracids. Experiments on α-phenyl-α,β-unsaturated ketones show that a mixture is produced, consisting mainly of α,β-unsaturated esters and a small amount of α,β-epoxy esters.

Performic acid oxidation of unsaturated materials ordinarily leads to good yields of the glycol or hydroxyformate. Performic acid, prepared and utilized *in situ*, however, has been used (350) successfully in epoxidation reactions. In this system, a minimum of formic acid (0.25-0.5 mole of formic acid per mole of unsaturation) is utilized to prevent cleavage of the epoxy ring caused by higher ratios of formic acid.

Recently (102, 149, 165), epoxidation techniques employing peracetic acid, formed and utilized *in situ*, have been developed. An important contribution has been the Du Pont development of using polystyrene sulfonic acid exchange resins to catalyze hydrogen peroxide in the epoxidation of unsaturated fats and oils. Referred to as the hydrogen peroxide-resin technique, this method eliminates the need for separate reactions, minimizes the acetic acid requirements, reduces by-products, and allows operation at higher temperatures. The method is an outgrowth of the discovery (407) that polystyrene sulfonic acid exchange resins catalyze the formation of peracetic acid in mixtures of glacial acetic acid and hydrogen peroxide.

The first modification of the resin technique for epoxidation has been described (95, 102, 149) as a simple batch system. In this system, hydrogen peroxide is charged to a mixture of unsaturated fatty oil, a small amount of acetic acid, and the polystyrene sulfonic acid resin catalyst. The reaction mixture is maintained at 60°-80°C. for 1-4 hours, then separated from the resin which is used in succeeding batches.

Considerable work (88, 146) on continuous processing under resin catalysis has been completed in the laboratory. This work began with the use of a simple column containing resin catalyst, from which evolved a system of circulating reactants (146), and finally became a procedure based on the cascade principle (88). At present the cascade process is the most promising method of continuous operation.

The resin technique has been adapted on a batch basis for the epoxidation of unsaturated glycerides, straight chain fatty esters, long-chain olefins (106), rubber-type polymers, and other unsaturated compounds. Maximum yields of epoxides are obtained by use of resin quantities of about 10% to 50% resin (dry weight) based on the weight of the unsaturated material. Decreasing resin amounts below 10% results in rapidly decreasing yields of epoxide under standard conditions and requires more vigorous reaction conditions to obtain suitable epoxy conversions. Use of about 2% resin based on the weight of the oil allows 75%-80% yields of epoxy soybean oil. Reaction times required at 75°-80°C., however, are two to five times greater than are required in the 10%-50% resin range (60°C.). Typical batch procedures for epoxidation often specify using 50% resin to insure good results on initial trials. In practice, equivalent results are obtained with a 10% to 12% resin catalyst ratio.

Other *in situ* epoxidation systems (103, 470) employing a strong acid such as sulfuric acid to accelerate reaction have been developed. Inert, hydrophobic solvents are often used to diminish the effect of the strong acid in producing cleavage and polymerization products.

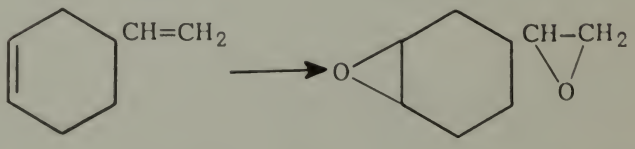
Polystyrene sulfonic acid exchange resins catalyze the formation of peracetic acid in mixtures of glacial acetic acid and hydrogen peroxide (407). Thus a safe, convenient, and economical method for the manufacture of peracetic acid at the site of operations consists of passing hydrogen peroxide and acetic acid through a cation exchange resin bed (150). The effect of the resin in this reaction is probably due to the acidity of the sulfonic acid function. Peracetic acid solutions obtained as effluent from this system are free of traces of acid

catalyst. Therefore, these peracid solutions are often suitable for epoxidation of compounds which form epoxides sensitive to rearrangement or cleavage by the resin or by strong acid catalysts used in *in situ* epoxidation techniques.

The surface effects (adsorption) of the resin in the resin technique, however, are important in obtaining a good epoxy yield. Since the adsorption process is rapid, a given quantity of oil appears to be epoxidized on the surface of the resin and removed rapidly. A fatty epoxide may not enter the free space of the resin bead to undergo epoxy cleavage because the absorption process (volume effect) is comparatively slow. If the nature of the resin or the epoxidizable material is such as to allow absorption by the resin, cleavage products may result. Porous exchange resins therefore are not desirable in epoxidation.

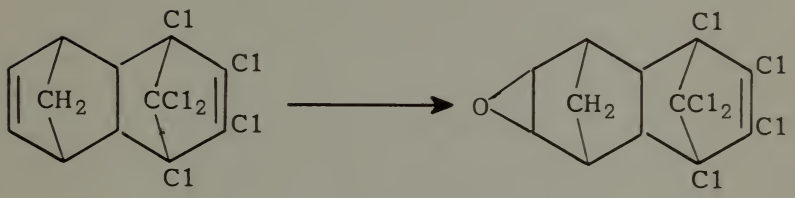
Peracetic acid in an inert solvent free of acetic acid has been used (461) to prepare styrene oxide in good yields. Commercial diisobutylene, consisting of an 80:20 mixture of the α- and β-isomers, has also been epoxidized effectively with this reagent. Other epoxides which have been prepared by use of peracetic acid in an inert solvent include vinylcyclohexene monoxide and dioxide, triisobutylene oxide, and the epoxides of various unsaturated nitriles,. alcohols, amides, ethers, and imides (368). Butadiene dioxide has been made from 1,4-dichloro-2-butene by epoxidation followed by hydrolysis and treatment with alkali.

Peracetic acid in acetic acid has been used to epoxidize 4-vinylcyclohexene (176) forming the dioxide in about 70% yields.



Epoxy polymers with possible uses as textile sizing or metal and leather finishing are prepared from the dioxide by a two-stage polymerization technique. Other diepoxides (186, 349) as precursors of molded and cast resins have also been prepared with peracetic acid.

Peracetic acid in acetic acid and perbenzoic acid have been extremely satisfactory in epoxidizing the Diels-Alder product (aldrin) of hexachlorocyclopentadiene and bicyclo-(2,2,1)-2,5-heptadiene (276, 294, 295, 426).



The epoxidized products are known commercially as dieldrin (endo-exo isomer) and endrin (endo-endo isomer). Aldrin, dieldrin, and endrin are general insecticidal compounds being active as stomach and contact poisons (214) for cotton, tobacco, fruit, and soil insect control. The incorporation of epoxy oxygen into aldrin confers increased insecticidal activity and decreased vapor pressure so that dieldrin and endrin have a residual action about equal to DDT.

Typical Procedure–Minimal Resin Technique

The following procedure employs 0.9% resin catalyst based on the weight of oil being epoxidized. Use of a minimal quantity of resin allows this catalyst to be discarded economically at the completion of each run. Use of 2% resin catalyst increases yields of epoxide somewhat.

Prepare a mixture of 40 g. of alkali refined soybean oil (iodine number 129.5), 0.36 g. of polystyrene sulfonic acid resin (medium porosity) containing approximately 0.08 g. (18%) of glacial acetic acid, and 7.7 g. of glacial acetic acid in a vessel equipped with a high speed stirrer, thermometer, and dropping funnel. While the mixture is being stirred vigorously, heat to 60°C. and add 15.2 g. of "Albone" 50 hydrogen peroxide over a period of 10 minutes. (Quantities larger than 40 g. of soybean oil will require correspondingly longer addition times.) Maintain the temperature at 60°C. by cooling with ice-water until the exotherm subsides (about 20-30 min. for 40 g. of soya oil). When the exotherm begins to subside,

raise the temperature of the reaction mixture to 75°-80°C. by heating in a water bath and maintain the reaction mixture at this temperature for about 7 hours. At the end of this time, cool the mixture in ice, and remove the resin by vacuum filtration. Collect the filtrate containing the product in 500 ml. of warm 1% NaCl solution. Separate the oily product layer, and then wash with 500 ml. portions of 1% NaCl, 5% $NaHCO_3$, 1% NaCl, and two 500 ml. portions of water. Dry the oil in a vacuum at 100°C. for 1 hour. If a cloudiness persists, add 2.5 g. of wood pulp filter aid ("Solk-a-flok") and filter. A light yellow product with an iodine value of 7.0 and an epoxy oxygen value of 6.11% (theory 7.48%) is obtained.

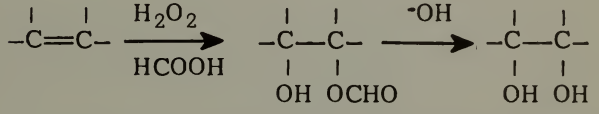
Typical Procedure—Repeated Resin Technique

The following procedure employs resin quantities in the range of 10% and 50% on the weight of epoxidizable matter. With soybean oil, the procedure imparts epoxy values between 6.5% and 7.0%. Epoxidized methyl oleate is obtained in yields up to 93%. Use of this amount of resin requires re-use of the catalyst in several succeeding batches for good economics.

Prepare a mixture of 29.6 g. (0.10 mole) of technical methyl oleate (iodine number 81.75), 18.0 g. of polystyrene sulfonic acid resin treated with 2.75 g. glacial acetic acid, and 0.55 g. of free glacial acetic acid (total acetic 0.055 mole) in a 100 ml. vessel equipped with a mechanical stirrer, thermometer, and dropping funnel. While the mixture is being stirred vigorously, add 7.48 g. (0.11 mole) of 50% hydrogen peroxide so that the temperature reaches 60°C. in fifteen minutes. Maintain the temperature at 60°C. for 2 hours, first with intermittent cooling by ice-water until the exotherm subsides and then by warming in a water bath. At the end of this time, cool the mixture in ice, and remove the resin by vacuum filtration. Collect the filtrate containing the product in 100 ml. of cold 1% NaCl solution. Separate the oily product layer, and then wash with 100 ml. portions of 1% NaCl, 5% $NaHCO_3$, 1% NaCl, and two 100 ml. portions of water. Dry the oil in a vacuum at 100°C. for 1 hour. A light yellow product (25 g.) with an iodine value of 6.81 and an epoxy oxygen value of 4.57% is obtained.

Hydroxylation

Practically the same procedures used in epoxidation are used also in hydroxylation except that strong acid catalysts and more vigorous reaction conditions are employed. Unsaturated substances have been hydroxylated quantitatively by peracetic acid, either preformed or prepared and utilized *in situ* (1, 438, 443). Quantitative yields of glycol have also been obtained (438, 444) with mixtures of formic acid and hydrogen peroxide. In most cases, the hydroxyacyloxy derivatives are isolated, but these are easily hydrolyzed to glycols by dilute alkali. It is difficult; however, to hydrolyze completely the hydroxyacyloxy derivative of glycerides without splitting the glyceride linkage.



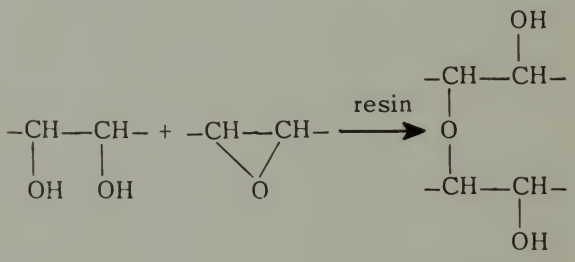
Solutions of acetic acid and hydrogen peroxide are used (499) commercially to hydroxylate natural mixtures of phosphatides (50%-70%) and oleaginous carriers known collectively as lecithin. The phosphatides have excellent emulsifying properties, but as lecithin are often dark colored, viscous, and difficult to disperse in water because of the presence of the oleaginous carriers such as soybean oil or cocoa butter. Removal of the oleaginous materials is undesirable because in their presence the phosphatides are stabilized against degradation by exposure to the atmosphere. Hydroxylation of the phosphatides at 50°-70°C. results in a product which is stable in the absence of the carriers and has increased hydrophilic properties in their presence.

As an emulsifier in chocolate manufacture, hydroxylated lecithin functions to wet the sugar of the chocolate with cocoa butter. This helps the chocolate to retain its gloss (anti-blooming) and to increase its keeping qualities.

Polymers such as liquid polybutadiene (MW<5000) have been hydroxylated with hydrogen peroxide-formic acid (153, 227). The products showing 2%-12% (by weight) of hydroxyl groups have possibilities as plasticizers and tackifiers for rubber, adhesives, and additives for drying oils.

Trifluoroperacetic acid has been reported (159) to be an effective reagent for hydroxylating olefins. The negatively substituted types such as allyl chloride and methyl methacrylate are also effectively hydroxylated by this reagent. The primary products formed are the hydroxytrifluoroacetates which are converted to vicinal glycols by saponification or methanolysis.

Methyl oleate has been converted (472) directly to methyl 9,10-dihydroxystearate with hydrogen peroxide and acetic acid, catalyzed by polystyrene sulfonic acid exchange resins of high porosity. Unlike other hydroxylation procedures, resin catalysis allowed the ester linkage to remain substantially intact. The dihydroxy derivative was obtained in yields up to 74%. By-products of the reaction consisted of small amounts of epoxide and a polymeric hydroxy ether. The polyether appears to be the product of the reaction of the glycol and epoxide formed transiently.



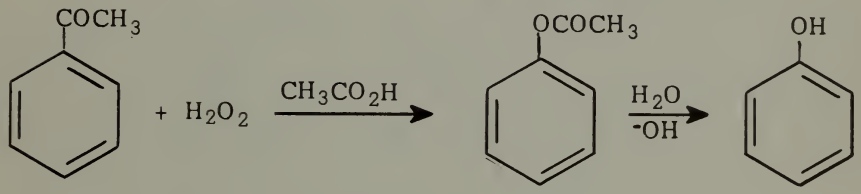
Polyether formation is catalyzed by porous exchange resins, but not by the less porous resins suitable for epoxidation. The reaction may be adjusted to produce polyethers exclusively.

Data obtained in developing this new technique tend to support the interpretation that resin catalysis in hydroxylation involves absorption of the fatty oil. Successful epoxidation probably requires that sorption of fatty oils be limited to adsorption on the surface of the resin.

Inorganic and organic peracids in a modification of the Dakin cleavage (126), which uses alkaline hydrogen peroxide, occasionally are used to convert ketone substituents of steroid rings to hydroxyl

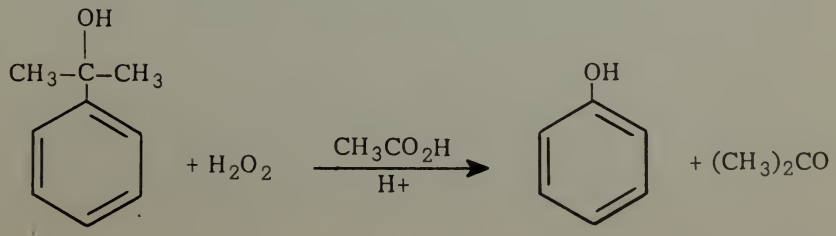
groups. Marker (305) has used this reaction for oxidizing methyl ketones of steroids to the corresponding esters. Obtaining the formerly unavailable pregnane compounds from sapogenins (304), Marker then was able to prepare 17-hydroxy-androstane derivatives and 21-hydroxy-20-keto-pregnane from 20-keto-pregnane compounds (303). Yields as high as 30%-45% for each of the two types of products were obtained in one simple step using hydrogen peroxide.

In a similar reaction, acetophenone yields phenyl acetate; benzophenone is oxidized quantitatively to phenylbenzoate (140). The hydroxy derivative is obtained by hydrolysis of the isolable ester produced by hydrogen peroxide oxidation.



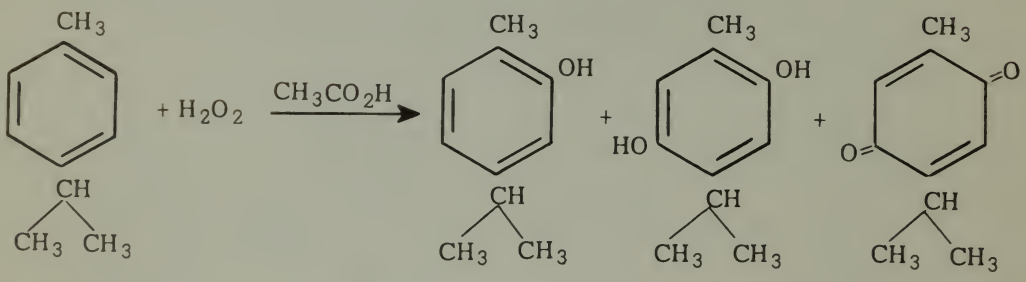
The reaction, in requiring a hydrolysis step, differs from the Dakin reaction where alkaline hydrogen peroxide converts aromatic aldehydes and ketones directly to the corresponding phenols in high yields.

Phenol can be prepared (400) in 85%-90% yields by reacting hydrogen peroxide and α,α-dimethylbenzyl alcohol in acetic acid solvent in the presence of sulfuric acid catalyst. Since acetone is also obtained in 85% yields in this reaction, it is probable that a hydroperoxide is first formed to be hydrolyzed to phenol and acetone in the presence of the strong acid.



Although this is not a true hydroxylation reaction, it is another method for manufacturing phenol; at present the demand for phenol far exceeds its manufacture from coal tar refining. Other available synthetic methods require greater equipment investments and involve many steps.

Aromatic rings have been hydroxylated directly with hydrogen peroxide in acetic acid. For example, 15% yields of oxidation products consisting of carvacrol, thymohydroquinone, and thymoquinone have been reported by Japanese workers (188) in the oxidation of p-cymene.



Typical Procedure for Hydroxylation (443)

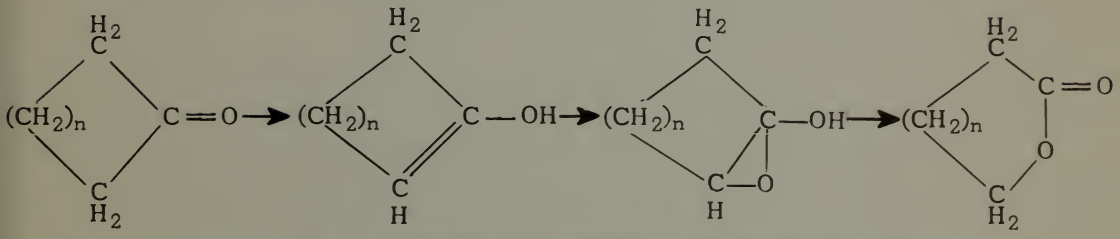
Mix 215 g. (0.898 mole based on iodine number of 101.7) of oleic acid, 60 g. (1.0 mole) of glacial acetic acid, and 3.7 g. of concentrated sulfuric acid. Add dropwise 68.2 g. (0.925 mole) of "Albone" 50 hydrogen peroxide. Maintain the reaction mixture at a temperature of 60°-70°C. for 3 hours. Pour the reaction mixture into hot water. Separate the light yellow oil in a separatory funnel and pour into excess 3N sodium hydroxide solution. Heat the clear, soapy solution at 90°C. for one hour. Then pour the solution into cold 4N hydrochloric acid and filter off the white solid. Wash free of acid with water, and air dry. The product (I.V. 9.7) is obtained in 90% yields.

Oxidative Cleavage – Ketones

Baeyer and Villiger (10) in 1899 found that solutions of hydrogen peroxide in concentrated sulfuric acid, allowed to form equilibrium mixtures of Caro's acid (H_2SO_5), oxidized cyclic ketones in

spectacular fashion to form lactones. This oxidation was particularly successful in the formation of 14- to 18-membered lactones. Hydrolysis of these lactones produces omega hydroxyaliphatic acids. Later it was shown that this reaction is a general one for organic peracids and related to the modified Dakin reaction discussed in the section on hydroxylation.

Since the oxidation of a cyclic ketone is effected by a peracid, Treibs (456) suggested that the reaction proceeded by way of (a) enol formation followed by (b) epoxidation of the enol. The best argument against this appears to be that in the oxidation of acetophenone to phenyl acetate, a similar reaction, there is no opportunity for enol formation.

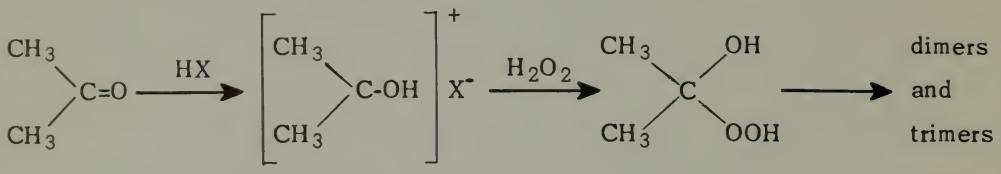


A convenient interpretation (180) of ketone cleavage is that the peracid adds directly to the carbonyl group forming an oxygen cation. Rearrangements of the oxygen cation may occur to form lactones or dimeric and trimeric peroxides (see below). Conducting ketone cleavage in the presence of ethanol may provide α-hydroxy esters directly.

The reaction of m- and p-substituted acetophenone with perbenzoic acid in chloroform to produce acetate esters (50%-80% yields) was found (185) to exhibit first order kinetics if the m- or p-substituents were electron attracting; second order if electron supplying. For both ketone types, however, the use of a more polar solvent accelerates the over-all reaction. The reaction was also found to be catalyzed by such weak acids as benzoic or acetic acid.

Most aliphatic ketones such as acetone or diethyl ketone react with peracids, especially Caro's acid, to produce unstable peroxides instead of esters. These peroxides are explosive and dangerous to handle. Many of them can polymerize to form

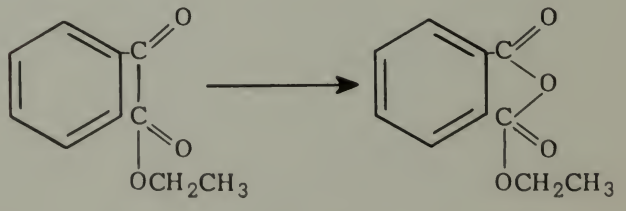
dimeric and trimeric peroxides. The reaction may depend upon the presence of small amounts of mineral acid to form carbenium salts (140) which react with peroxide directly.



Certain aliphatic ketones such as pinacolone and mesityl oxide tend to form esters in lieu of the peroxides mentioned above. Treatment of mesityl oxide with peracetic acid probably results (481) in a mixture of the α,β-unsaturated ester and the α,β-epoxy ketone derivatives.

Trifluoroperacetic acid converts (156) most ketones to esters in excellent yields. The products are generally obtained uncontaminated by the starting ketones. Transesterification is avoided during the oxidation by using dibasic sodium phosphate to remove trifluoroacetic acid as formed. The reaction is carried out by the addition of the peracid to a refluxing solution of the ketone in methylene chloride in which the phosphate has been slurried.

Karrer and Haab (258) have demonstrated that α-diketones, o-quinones, and α-ketocarbonic acid esters are oxidized to anhydrides by monoperphthalic acid in ether.



Under appropriate conditions, diketones and quinones are cleaved to carboxylic acids by peracid systems. Boeseken and Sloof (54) have produced 90%-95% yields each of azelaic and pelargonic acids from 9,10-diketostearic acid with peracetic acid; about a 76% yield of o-carboxyallocinnamic acid from β-naphthoquinone.

$$CH_3(CH_2)_7COCO(CH_2)_7COOH \longrightarrow CH_3(CH_2)_7COOH + HOOC(CH_2)_7COOH$$

Cleavage of diacetyl with peracid to form two moles of acetic acid proceeds violently; cleavage of benzil to benzoic acid under similar conditions is much slower. Other investigations on the action of hydrogen peroxide in acetic acid on α,α-diketones and quinones are noted by Perkin (365). Phenanthrene quinone, for example, yielded pure diphenic acid.

Peracetic acid also cleaves (51) 1,3-dicarbonyl compounds to produce secondary alcohols and pyruvic acid derivatives. Further oxidation in the presence of excess peracid may also occur. Because of the possibility of consecutive reactions, the nature of the products which may be obtained cannot always be predicted as they can be in the oxidation of α-dicarbonyl compounds.

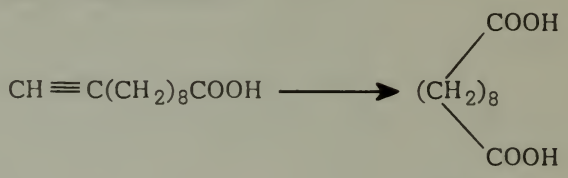
Oxidative Cleavage–Unsaturated Bonds

Many of the reactions of the hydrogen peroxide-peracid systems may be considered cleavage reactions. Those involving functional groups are discussed under the appropriate headings. Other oxidative cleavage reactions include cleavage of olefinic and acetylenic bonds.

Vitamin A aldehyde has been obtained (241) in very small yields (0.5%) by cleavage of the middle bond in β-carotene with peracid. Much higher yields (30%) have been obtained (313, 326, 480) with metal activated systems.

Prileschajew (374) first investigated the action of a peracid on an acetylenic bond. He obtained surprisingly enough the methyl ester of phenylacetic acid by reacting phenylacetylene and perbenzoic acid. Phenylacetylene was not attacked by peracetic acid. To vitiate the effect of the phenyl ring, Boeseken and Sloof (55) studied the reaction of peracetic acid with stearolic, 9-undecolic, and 10-undecolic acids. Over long reaction periods (1-7 weeks at room temperature), these acids were cleaved to produce azelaic and pelargonic acids (60% yields), a small amount of suberic acid, and sebacic acid.

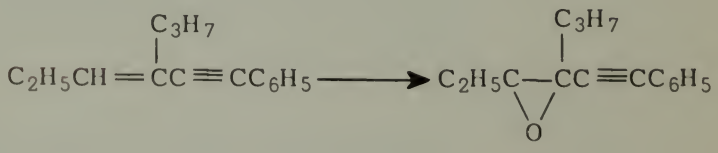
The reaction was presumed to involve hydroxylation of the acetylenic bond followed by the formation and cleavage of an α,α-dicarbonyl compound. The reaction is shown below:



10-undecolic acid *sebacic acid*

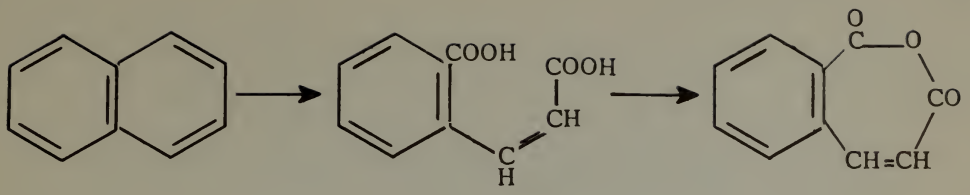
Acetylenic compounds have been reported (178, 406) to react with peracetic acid yielding acetylene oxides. Although the oxides may be the primary products, the products isolated in this reaction are α,β-unsaturated ketones formed in the rearrangement of the oxide.

Butynediol and peracids react (179) to form malonic acid. The α,β-unsaturated ketone or its tautomer is assumed to be an intermediate in this oxidation. Under certain conditions acetylenic hydrocarbons and peracetic acid react (177, 405) to give cleavage products consisting mainly of carboxylic acids. Russian workers (302) have reported that peracetic acid epoxidizes the olefinic portion of the vinyl acetylenic compound, 4-phenylethynyl-3-heptene, leaving the acetylenic bond intact.



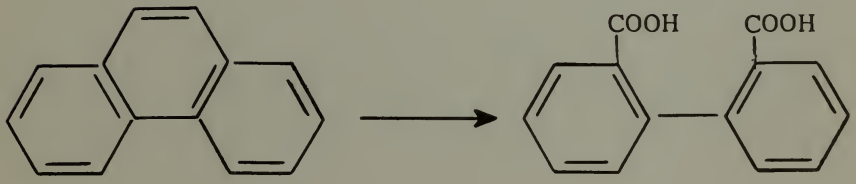
Oxidative Cleavage – Aromatic Rings

Aromatic rings react with peracetic acid to yield cleavage products. Benzene itself is very stable to peracids unless it is first converted to phenol or quinone. In this case, cis,cis-muconic acid is formed (49, 50, 58, 467). Naphthalene reacts (56) slowly with peracetic acid at room temperature producing o-carboxyallocinnamic acid which may form the anhydride by splitting off water.



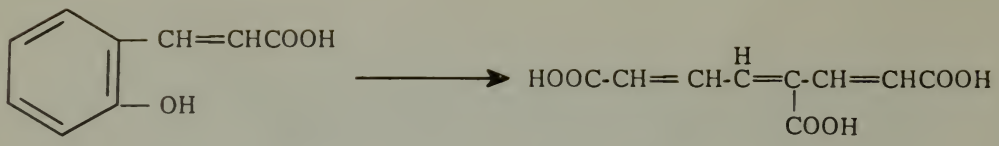
Both α- and β-naphthol are cleaved (58) to the o-carboxycinnamic acid, β-naphthol giving slightly higher yields.

Phenanthrene reacts (132) rapidly with hydrogen peroxide in acetic acid to give 42% yields of diphenic acid useful in plasticizer and alkyd resin manufacture. Although an abundant raw material, phenanthrene is not easily separated from anthracene and carbazole in the distillates of coke-oven and horizontal retort tars. Isolation of phenanthrene is difficult because of its high solubility in tar oils and its tendency to form mixed crystals with other polynuclear compounds of similar boiling points. Otherwise phenanthrene is an excellent raw material for oxidation reactions. Cleavage of phenanthrene with preformed peracetic acid has produced as high as 70% yields (353) of diphenic acid.



Unreactive in the liquid phase, phenanthrene is oxidized by air over V_2O_5 at 400°C. to form the anhydride. Oxidative hydrolysis of the anhydride with hydrogen peroxide-acetic acid results in 70% yields of diphenic acid.

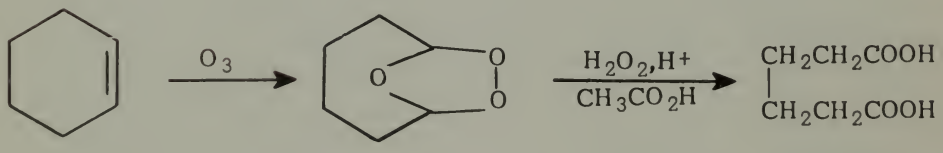
Grundmann and Trischmann (211) attempted to obtain aliphatic polyene polycarboxylic acids by the action of peracetic acid on certain substituted phenols. Thus 1,4,6-hexatrienetricarboxylic acid was expected to result from the oxidation of o-coumaric acid.



However, muconic acid, $HOOC(CH{=}CH)_2COOH$, was the chief product isolated.

Oxidative Ozonolysis

A reliable (169, 190, 234, 308) procedure for the oxidative cleavage of double bonds involves the addition (422) of ozone (ozonization) followed by hydrolysis of the ozonide (ozonolysis). Henne and Hill (224) describe procedures for obtaining aldehydes, ketones, and carboxylic acids by ozonolysis. To be converted to aldehydes, the ozonide is allowed to undergo reductive ozonolysis in a mixture of zinc and acetic acid. In the ordinary acid hydrolysis of ozonides, a considerable amount of aldehydes is formed in some cases along with the carboxylic acids. To be converted completely to carboxylic acids, the ozonide solution is dropped slowly into a mixture of acetic acid and hydrogen peroxide. Thus by oxidative ozonolysis with hydrogen peroxide, cyclohexene is converted in 60% yields to adipic acid.



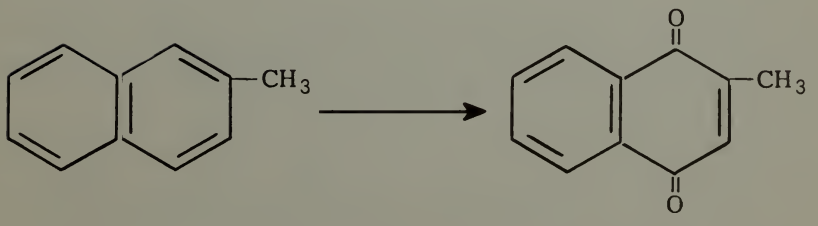
Typical Procedure for Oxidative Ozonolysis (224)

Prepare a solution of 6-methyl-1-heptene in 200 ml. of methylene chloride. Cool the solution to -78°C. and introduce a stream of ozonized oxygen at the rate of 20 liters per hour for 12 hours. By suction remove the solvent from the ozonide and replace with 100 ml. of acetic acid. Allow the resulting ozonide solution to drip into a mixture of 114 g. of 30% hydrogen peroxide, 5 ml. of concentrated sulfuric acid, and 200 ml. of water contained in a 1-1 round-bottom flask fitted with a dropping funnel, a sealed stirrer, and a reflux condenser.

Heat cautiously and progressively. If the reaction becomes vigorous, apply intermittent cooling. Continue refluxing for 2 hours and extract with ether after cooling the reaction mixture to an ice temperature. Extract the ether layer with an aqueous solution of sodium hydroxide. Acidify the aqueous sodium hydroxide layer and again extract with ether. Dry the ether layer and distill. Collect the 5-methylhexanoic acid at 200°-210°C.; then redistill. Yields average 67%.

Quinone Formation

Because of the great number of investigations on bacterial metabolism, carcinogenic substances, and vitamins (E, K_1, and K_2), there is increasing interest in the manufacture of quinones. The oxidation of polynuclear hydrocarbons by hydrogen peroxide results in a clean and efficient process for the preparation of quinones and substituted quinones. The reaction is operated at somewhat elevated temperatures (80°-125°C.) and requires a solvent such as acetic acid which does not cause the decomposition of the products. The reaction is particularly useful for the preparation of 2-methyl-1,4-naphthoquinone (7) having vitamin K activity. Vitamin K differs from this material structurally in having a phytyl side chain in the 3-position. In vitamin K therapy 2-methyl-1,4-naphthoquinone and certain simple derivatives are as effective antihemorrhagic and bacteriostatic agents as vitamin K itself. It may be that the phytyl group is supplied in the organism (191).



Durene, naphthalene and derivatives, benzanthracene, and pyrene have all been converted to quinones in good yields by Arnold (7). With excess peracetic acid, quinones are cleaved to dicarboxylic acids (54). Anthraquinone is not prepared commercially by the oxidation of anthracene because of the difficulty of obtaining anthracene from coal tar.

Anthracene, however, has been oxidized to anthraquinone in 70% yields by a modification of Arnold's method (208). Anthraquinone is generally produced by a Friedel-Crafts condensation of benzene and phthalic anhydride in the presence of $AlCl_3$. Recently dimethylacetamide has been shown to be a good solvent for separating anthracene and carbazole in coal tars by selectively dissolving the carbazole. Anthracene, therefore, may take its place with naphthalene and benzene as starting materials for anthraquinone mordant and vat dyes.

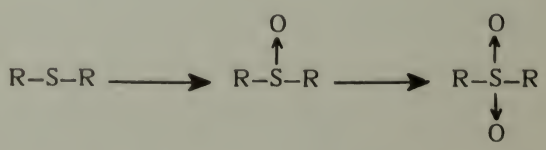
Typical Procedure for Quinone Formation (7)

To 5.0 g. of 2,3-dimethylnaphthalene in 75 ml. of glacial acetic acid at 50°C., add 15 ml. of 30% hydrogen peroxide and allow to stand at 80°C. for 10 hours. After an induction period, the solution turns yellow and then gradually develops a cherry red color. Evaporate the solvent and steam distill the residue obtaining a 78% yield of 2,3-dimethyl-1,4-naphthoquinone, melting point 127°C.

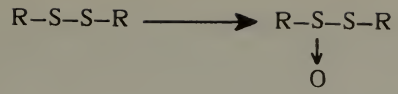
Organic Sulfur Oxidation

Compounds containing the sulfhydryl group (mercaptans) are readily oxidized to disulfides by mild oxidizing agents. Stronger oxidizing agents are capable of transforming mercaptans directly to the highly oxidized sulfonic acids (250). Peracids are stronger oxidizing agents than aqueous hydrogen peroxide and are, therefore, rarely used to prepare disulfides.

Sulfides and disulfides are oxidized rapidly and efficiently by peracids or hydrogen peroxide in acetic acid. Sulfoxides are produced by one mole of hydrogen peroxide, sulfones by two.

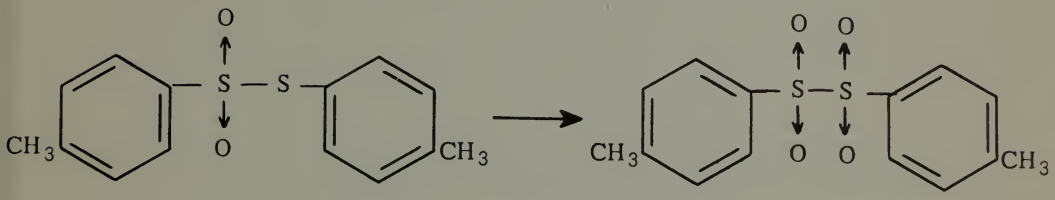


Although peracid systems are most useful for the preparation of sulfones (245, 270, 288, 372, 404, 452) in almost quantitative yields, sulfoxides of both sulfides and disulfides have been prepared with peracids.



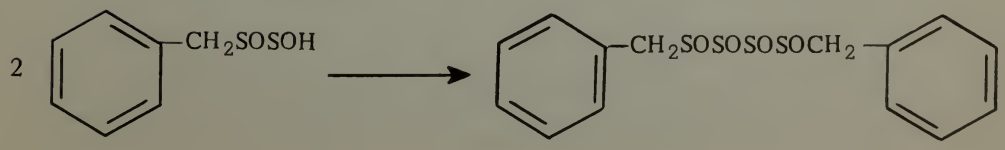
Hypnotic agents (372) and low-toxicity anti-convulsants (297) have been prepared by converting sulfides to sulfones. The sulfoxides of disulfides apparently provide the antibacterial factor in garlic. They are prepared (419) with hydrogen peroxide in acetic acid in 20%-65% yields.

Thiolsulfonic esters like di-p-tolyl disulfoxide are converted (202) by peracetic acid to the disulfones.



The thiolsulfonic ester may first be hydrolyzed to sulfenic and sulfinic acids by hydrogen peroxide which then are oxidized to α-disulfones. However, an investigation (202) of this point proved that these esters are not hydrolyzed under the conditions employed in the reaction; the sulfur atom is oxidized directly. A table by Swern (437) lists the organic sulfur compounds converted to sulfoxides and sulfones.

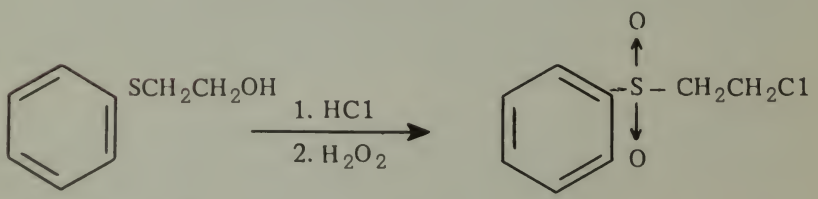
The possibility of hydrolysis of polysulfides by peroxide was also recognized by Smythe (424) who obtained the tetrasulfoxide in about 50% yields by treating dibenzyl trisulfide with hydrogen peroxide in acetic acid. In this case, the hydrolysis products of the trisulfoxide are the sulfinic and sulfoxylic acids. Oxidative condensation of the sulfoxylic acid produces the tetrasulfoxide in the yields indicated.



Alicyclic sulfur compounds are oxidized smoothly by peracid. Thus, 1,4-dithian is converted (29) to the disulfoxide in 95% yields.

Trimethylene trisulfide similarly is converted (30) to the monoxide or the various geometrical isomers of the dioxide and the trioxide.

Polymers containing the thioether linkage are susceptible to oxidation by peracids. The polyamide thioether of hexamethylene diamine and 4-thiapimelic acid has been oxidized (170) to the sulfone derivative by hydrogen peroxide in formic acid. This polymer is a nylon counterpart containing sulfone functions. Polymeric sulfones have also been prepared (351) by the action of the above reagent on polyhexamethylene sulfide. The use of concentrated formic acid allows the oxidation products to remain in solution until oxidation has proceeded to the sulfone stage. Free of comparatively unstable sulfoxide groups, polysulfones have superior physical properties including greater thermal stability and enhanced fiber-forming characteristics. Vinyl sulfones as monomers for copolymerization are prepared by dehydrohalogenating the following sulfone (288):

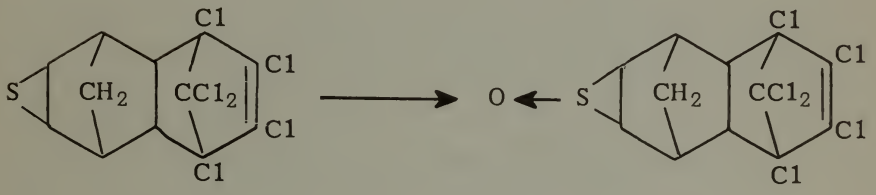


The starting material is prepared by condensing thiophenol and ethylene chlorohydrin.

Squalene (acyclic dihydrotriterpene), combined with sulfur to form a sulfur-rich product serving as a model for ebonite (hard rubber), can be desulfurized (245) by acetic acid and hydrogen peroxide. Desulfurization apparently also occurs with natural rubber combined with sulfur in high-sulfur vulcanization. The reaction of these unsaturated materials with sulfur may not be confined to the double bonds. The sulfur content often corresponds to two sulfur

atoms per double bond including 15% of the original unsaturation which survives vulcanization.

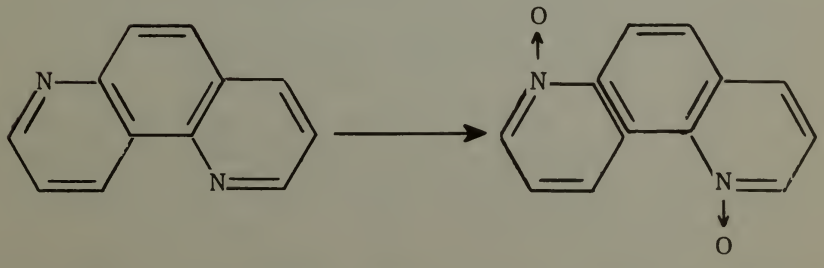
Aldrin, which undergoes increased insecticidal activity upon epoxidation, has been treated with peracids in another way to form a sulfoxy insecticide (47, 427). Treating aldrin with (a) bromine and (b) sodium sulfide produces the 6,7-episulfido compound. Upon reaction with peracetic acid, the episulfido derivative is converted to the insecticidal 6,7-episulfoxy derivative.



This material, obtained in both the endo-endo and exo-endo configurations, has also been found toxic to rodents.

Organic Nitrogen Oxidation

Organic nitrogen compounds are easily oxidized with peracids, not so effectively with aqueous hydrogen peroxide systems. Tertiary amines can be suspended in aqueous medium and then reacted (166) with hydrogen peroxide to produce nitrogen oxides. This method is generally characterized by a slow rate of reaction. Tertiary amines, often of the condensed ring type, are more effectively oxidized (163) by peracids.



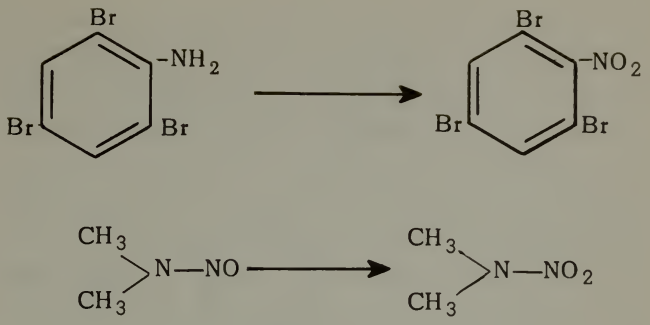
Heterocyclic nitrogen oxides prepared in this way are finding use in medicinal preparations as substitutes for ternary bases.

Experiments conducted (377) with perbenzoic acid have shown that the rates of oxidation of tertiary amines, alicyclic double bonds, and aromatic rings are in the order listed. In compounds containing all three functional groups, monoperphthalic acid can be used to convert the tertiary amino group to the amine oxide without epoxidizing the double bond or cleaving the aromatic ring.

The oxidation of nitrogen compounds up to now has enjoyed little commercial potentiality because of the variety of products obtained in such oxidations. For example, the products of the oxidation of primary amines with hydrogen peroxide ordinarily are mixtures of hydroxylamines, azo, azoxy, nitroso, and nitro compounds. The reactions of primary aromatic amines and peracids, however, usually produce nitroso or nitro derivatives although the by-products mentioned above may be present in considerable quantities (13, 42, 129, 208, 373, 417). The fact that nitrogen oxides provide new and improved drugs (105) has spurred commercial interest in techniques involving hydrogen peroxide to oxidize nitrogen heterocyclic compounds.

All varieties of nitrogen compounds appear to respond to peracids. Secondary amines are converted (145, 417) to di-N-substituted hydroxylamines. Azo compounds are oxidized smoothly to azoxy derivatives in quantitative yields although reaction often proceeds slowly (71, 289, 437). Phenylhydrazones are transformed by perbenzoic acid (301) to nitrosobenzene and acetophenone derivatives. Mixtures of nitric acid, hydrogen peroxide, and acetic acid constitute excellent reagents for oxidizing aromatic nitroso compounds to the nitro form in yields ranging to 88% (286). This method is especially valuable when alkyl substituents, sensitive to oxidation, are desired intact.

Trifluoroperacetic acid oxidizes oximes to nitroparaffins (158) in the presence of acetonitrile, anilines to nitrobenzene, and nitrosamines to nitramines (155).



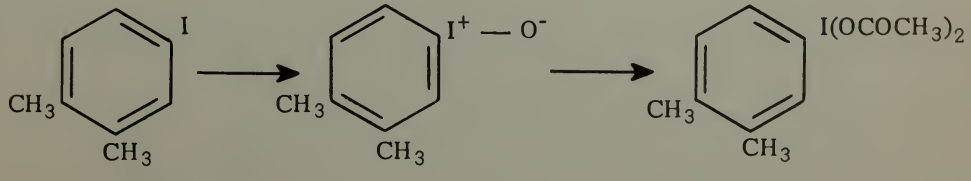
A few aniline derivatives added (428) to peracetic acid solutions treated beforehand with sodium bisulfite curiously produced high yields of acetylated products.

Typical Procedure for the Oxidation of Tertiary Nitrogen (462)

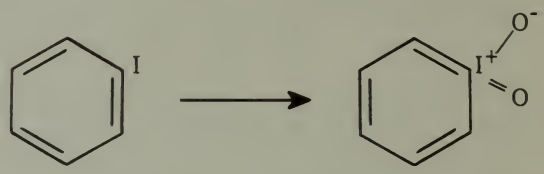
Add 100 ml. of 30% hydrogen peroxide to 100 g. 6-methoxyquinoline in 700 ml. of glacial acetic acid at room temperature. Maintain the reaction temperature at 50°C.; then distill the reaction mixture to 1/2 volume. Add 200 g. of ice and 75 ml. of a 40% aqueous solution of sodium hydroxide. The 6-methoxyquinoline-N-oxide precipitates in approximately 90% yields.

Oxidation of Organic Iodine Compounds

Peracetic and perbenzoic acids have been used to prepare polyvalent iodine compounds, in certain instances in about 90% yields (5, 53, 59). Aromatic and aliphatic iodine compounds alike are oxidized with peracetic acid in acetic acid usually forming iodosodiacetates. The iodoso compound is presumably the primary product.



Used with inert solvents or buffered systems, peracetic acid can be employed to form the iodoso derivative. The iodoxy derivative is prepared by oxidizing iodosodiacetates or the iodo compound directly with perbenzoic acid.



Certain iodoxy compounds apparently are reconverted to the iodosodiacetate derivative by peracetic acid in acetic acid (5).

The solubility of phenyliodoso dipropionate in light petroleum and the behavior of phenyliodoso diacetate as an undissociated molecule in solvents of varying polarity suggest (249) covalent structures (I) rather than ionic structures (II) for these materials.

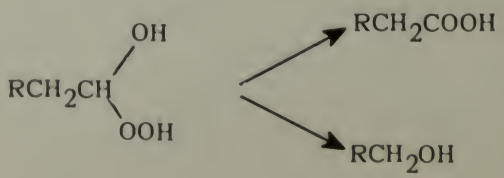
$$RI(OCOR)_2 \qquad (RIOCOR)^+ \; RCOO^-$$

(I) (II)

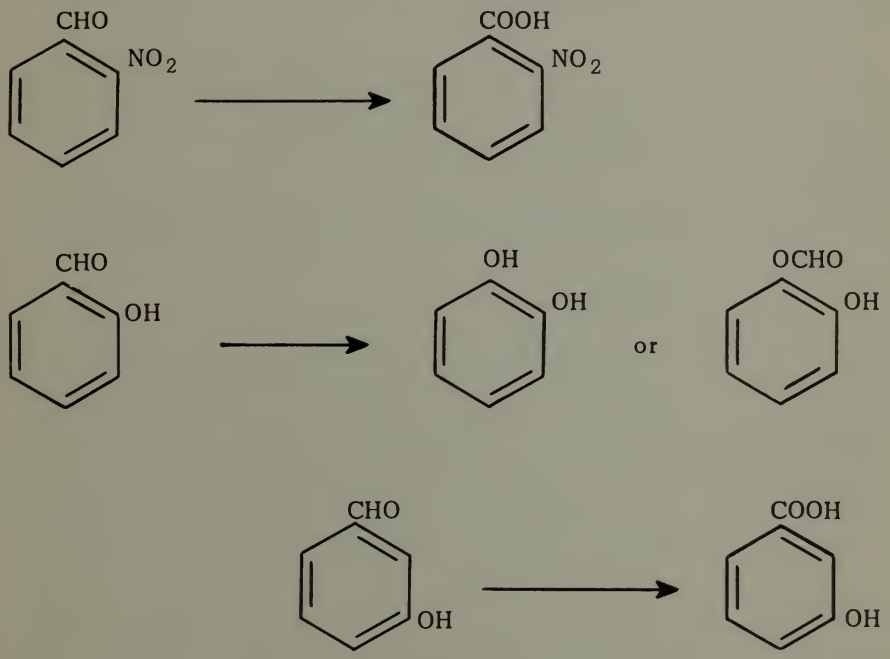
Iodosobenzene diacetate and related compounds are oxidizing agents similar to lead tetraacetate in their reactions. Iodosobenzene diacetate is an effective agent for cleaving α-diols in 1,4-diradical reactions and oxidizing (418) monovalent phenols to quinolacetate, methylolacetate, and quinones.

Oxidation of Aldehydes

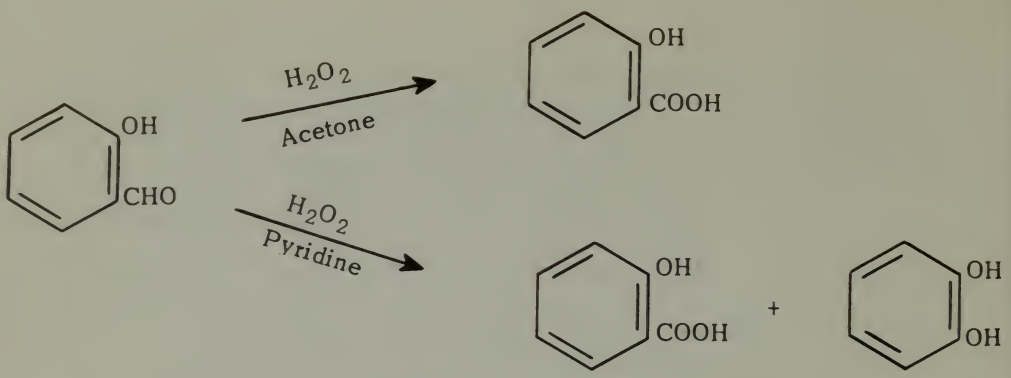
The reaction of aldehydes and hydrogen peroxide is believed to form a hydroxy hydroperoxide as a primary product. The peroxide, being unstable, is converted to alcohols or carboxylic acids.



Aliphatic aldehydes reacting with peracids almost always form carboxylic acids. The products formed by the oxidation of aromatic aldehydes depend generally upon the substituents found on the aromatic rings, and both carboxylic acids and alcohols are found. The oxidation of benzaldehyde by peracids results in higher yields of benzoic acid than of phenol. With such meta-directing substituents as nitro groups, carboxylic acids are usually the only products isolated. In reactions involving electron-releasing substituents ortho or para to the carbonyl function, alcohols or formyl esters are produced in high yields.



Although hydrogen peroxide in acetic acid converts salicylaldehyde to pyrocatechol, the use of organic solvents other than acetic acid results in different products despite the presence of the vicinal hydroxyl group. Hydrogen peroxide-acetone gives quantitative yields of salicylic acid; hydrogen peroxide-pyridine, 75% salicylic acid and 20% pyrocatechol.



Aliphatic and aromatic aldehydes alike often form hazardous peroxides with Caro's acid. The reactions of chloral and benzaldehyde with Caro's acid are examples.

The oxidation of aldehydes with peracids has not been used widely for preparative purposes. Therefore, such reactions have little commercial significance at the present time.

A fairly comprehensive review of the oxidation of aldehydes and ketones is given by Hudlicky (239).

Oxidation of Alcohols

Alcohols and peracids, usually mixtures of hydrogen peroxide and concentrated sulfuric acid, may react to form organic peroxides. Such reaction mixtures, especially those involving the lower secondary and tertiary alcohols, have exploded (451). The risk of explosions is increased by use of concentrated peracids. Tertiary butyl alcohol forms (337) t-butyl hydroperoxide and smaller amounts of di-t-butyl peroxide in reacting with 27% hydrogen peroxide in 70% sulfuric acid. Tertiary aromatic alcohols may be converted to cleavage and rearranged products; diphenyl-o-tolyl carbinol gave (265) 2-methyl phenol, benzophenone, and unidentified products. An organic peroxide intermediate probably is formed and rearranged under conditions for acid hydrolysis.

ALKALINE HYDROGEN PEROXIDE SYSTEMS

The reactions of hydrogen peroxide in alkaline media are apparently those of the hydroperoxide anion (74, 75, 486).

$$H_2O_2 + {}^-OH \longrightarrow {}^-OOH + H_2O$$

It is the action of this anion which often makes the reactions of alkaline peroxide different from peracid reactions. The difference becomes apparent on considering the epoxidation reaction. Compounds such as α,β-unsaturated ketones are effectively epoxidized by the alkaline reagent. Peracids, however, convert these ketones to esters. The active reagent in alkaline hydrogen peroxide, therefore, is probably sodium hydrogen peroxide.

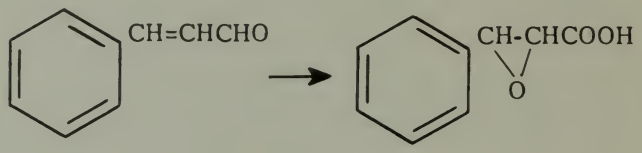
The alkaline reactions of hydrogen peroxide have been carried out in water, aqueous alcohols, aqueous acetone, and other solvents. A simple method of using a water-alcohol solution consists of adding hydrogen peroxide and aqueous alkali or carbonate solution to a solution of the organic substrate in alcohol (165, 453). A slightly alkaline solution of hydrogen peroxide can be prepared (279) by adding one mole (80 g.) of sodium peroxide slowly to a mixture of ice and water (650 g.) in a salt-ice bath. Concentrated hydrochloric acid (1.7 moles) is then added at 5°C. to reduce alkalinity. If the resulting solution is to be used in an alcoholic medium, a small amount (50 ml.) of alcohol is added immediately to stabilize the solution and to help prevent precipitation of the organic reactant. The use of hydrogen peroxide in lieu of sodium peroxide in organic work, however, is strongly recommended.

Hydrogen peroxide in alkaline solutions is susceptible to decomposition, especially under the influence of such contaminants as heavy metals. The presence of traces of heavy metals may also cause side reactions. Therefore, the reduction of alkalinity to its lowest effective point, the avoidance of contamination, and the use of proper equipment are desirable for efficient use of the alkaline peroxide system.

From a safety standpoint, the use of anhydrous or water-free alcoholic or acetone solutions of hydrogen peroxide should be avoided. The presence of water tends to desensitize dangerous organic hydrogen peroxide mixtures.

Epoxidation

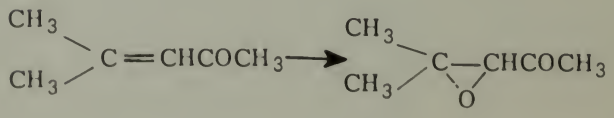
Alkaline hydrogen peroxide is effective (476) in epoxidation of α,β-unsaturated carbonyl compounds and nitriles. Nitrile and aldehyde functions in such molecules may be oxidized further, however, to amides and acids respectively during epoxidation. Cinnamaldehyde, for example, is converted to the glycidic acid derivative.



α,β-Unsaturated acids such as cinnamic acid and conjugated olefins are not epoxidized by alkaline peroxide.

Oxidizing agents other than alkaline peroxide tend to cleave α,β-unsaturated carbonyl compounds at the olefin linkage. Cinnamaldehyde under attack by general oxidizing agents yields benzoic acid. Peracids, however, do not epoxidize α,β-unsaturated compounds which are so readily converted to epoxides by alkaline hydrogen peroxide. Alkaline peroxide reagent, on the other hand, does not attack isolated double bonds which respond to peracids.

Weitz and Scheffer (476) first (1921) used alkaline peroxide solutions in the epoxidation of materials like mesityl oxide and the benzal ketones. Mesityl oxide epoxide was previously prepared by the action of potassium carbonate on mesityl oxide chlorohydrin.

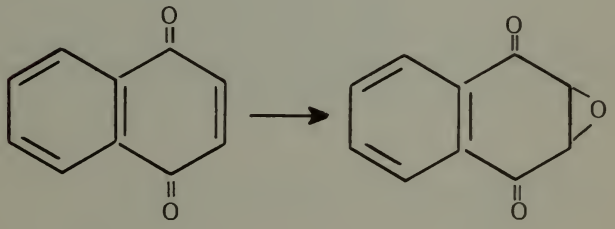


The peroxide system employed by Weitz and Scheffer required the use of an organic solvent under homogenous reaction conditions. The use of aqueous alkaline medium (491), however, eliminated the need for reaction and extraction solvents and increased

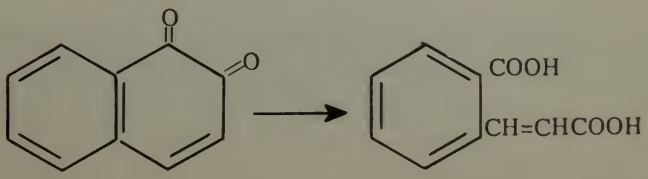
the yield of epoxide. Reactions conducted (75, 141, 346, 347) in aqueous mixtures also tend to give fewer by-products to contaminate the epoxide. Epoxy mesityl oxide, ordinarily considered unstable to heat, appeared to be very stable (491) when prepared in aqueous alkaline medium.

Although the use of aqueous alkaline peroxide solutions is desirable in epoxidation, the alcoholic solutions of Weitz and Scheffer are satisfactory in many instances. Thus benzalacetophenone oxide (279) is prepared in 85% yields by use of sodium peroxide in aqueous alcoholic reaction medium. Other alkaline systems of hydrogen peroxide employed successfully in epoxidation include those involving methanol (236), ethanol (279), pyridine (476), and dioxane (91) solvents.

Such quinones as naphthoquinone are epoxidized by alkaline peroxide producing the 2,3-oxide in good yields. The reaction is carried out by mixing naphthoquinone dissolved in methanol with 30% hydrogen peroxide and 2N sodium hydroxide (478).



1,2-Naphthoquinone, however, is cleaved by alkaline peroxide to form the o-carboxycinnamic acid.



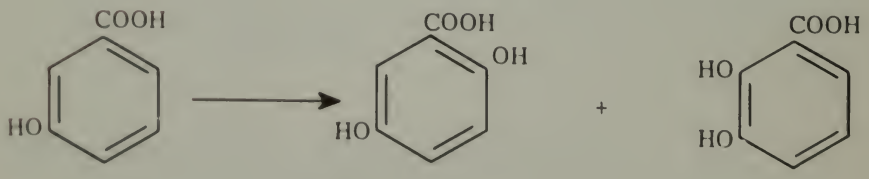
Typical Procedure for Epoxidation (491)

Cool mesityl oxide (100 g.) below 10°C. Stir in a solution of sodium hydroxide (4 g.) in water (150 ml.), and add magnesium sulfate (1.25 g.) to aid in precluding side reactions. Add 35% hydrogen peroxide (165 g.) over 30 minutes maintaining reaction temperature below 30°C. and agitate the reaction mixture for 30 to 60 minutes after peroxide addition has been completed. Add sodium sulfate (100 g.) and allow the mixture to stand for one hour to separate the aqueous and organic layers. Distillation of the upper layer produces the product in 87% yields.

Hydroxylation

Alkaline hydrogen peroxide is not ordinarily a reagent for hydroxylation except in the sense of preparing hydroxy products through intermediate epoxy rearrangement (477) reactions. However, the Elbs oxidation (18), employing alkaline potassium or ammonium persulfate, is a common reagent for hydroxylation of aromatic rings.

Potassium persulfate is apparently more reliable (175) than ammonium persulfate for hydroxylating m-hydroxybenzoic acid in the Elbs reaction. Gentisic acid is the predominant product in this reaction although small amounts of catechuic acid are also found.



gentisic acid *catechuic acid*

The nuclear oxidation of coumarins by alkaline persulfate introduces (92) a hydroxyl group into the 6-position. When this position is occupied, either no oxidation takes place or an abnormal reaction results.

Oxidative Cleavage – Ketones

The facile cleavage of twinned carbonyl compounds, ketoacids, and polyketo compounds by alkaline peroxide testifies to the existence of the active hydroperoxide ion (^-OOH). Cleavage of these materials, almost always producing carboxylic acids, is believed (74) to involve the hydroperoxide ion in the rate-determining step. The use of alkali (^-OH) alone usually does not result in cleavage products.

Benzil treated with alkaline peroxide produces benzoic acid.

$$C_6H_5COCOC_6H_5 \longrightarrow 2C_6H_5COOH$$

Most aromatic and a few aliphatic diketones, in contrast, undergo the benzilic acid rearrangement under influence of alkali.

$$C_6H_5COCOC_6H_5 \xrightarrow{^-OH} (C_6H_5)_2\underset{\displaystyle OH}{\overset{\displaystyle |}{C}}CO_2Na$$

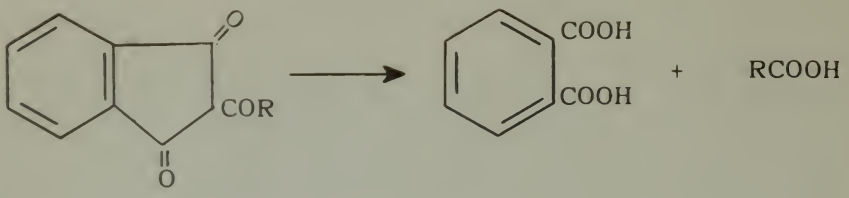
benzil *benzilic acid salt*

The oxidation of α-ketoacids to yield carboxylic acids is effected conveniently (226) in alkaline peroxide; thus benzoylformic acid rapidly yields benzoic acid.

$$C_6H_5COCOOH \longrightarrow C_6H_5COOH$$

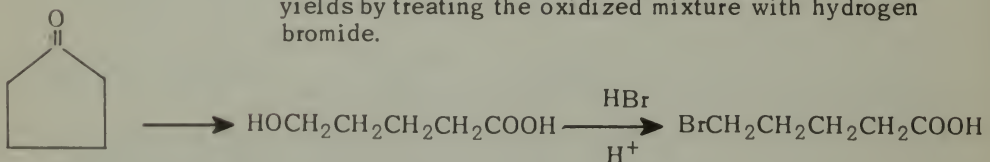
Many α-ketoacids warmed gently with concentrated sulfuric acid, eliminate carbon monoxide resulting in carboxylic acids. However, some aliphatic α-ketoacids are decomposed by heating with 10% sulfuric acid, producing aldehydes. Hydrogen peroxide tends to convert all α-ketoacids to carboxylic acids.

Symmetrical triketones have been cleaved (217) rapidly to carboxylic acids by hydrogen peroxide in either alkali or sulfuric acid. Thus 1,3-diketo-2-acyl indane produced phthalic acid and the carboxylic acid corresponding to the acyl moiety.



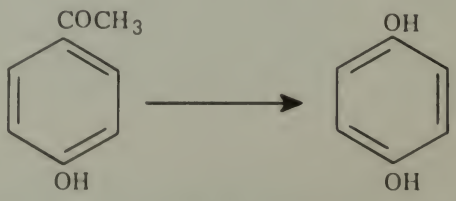
A hydroxy hydroperoxide may have been formed as an intermediate. Curiously, peracetic and perbenzoic acids are reported as having been ineffective in cleaving these compounds.

Like Caro's acid and peracids, alkaline hydrogen peroxide has been used to cleave alicyclic ketones. Unlike the inorganic or organic peracids, however, alkaline peroxide does not permit isolation of lactones as products of the reaction. Hydroxy acids are formed directly although Westerfield (483) has reported isolation of the lactone following alkaline oxidation of cyclopentanone. Isolation of ϵ-caprolactone was unsuccessful in later efforts (171,223) to oxidize cyclohexanone. However, ϵ-bromocaproic acid was obtained in 19% yields by treating the oxidized mixture with hydrogen bromide.



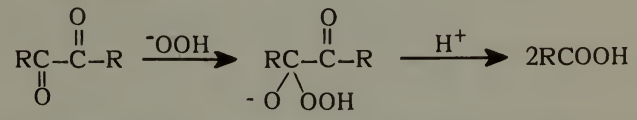
Explosions resulted in several instances during attempts to isolate lactones even though excess peroxide had been destroyed with sodium bisulfite.

Hydrogen peroxide solutions containing ammonia have cleaved o- and p-hydroxy and methoxy acetophenones to the corresponding catechols.



The reaction is similar to Dakin's use of alkaline peroxide on phenolic aldehydes and to the use of peracids to convert aromatic ketones to esters.

Hydrogen peroxide, once considered to react upon twinned carbonyl compounds and ketoacids by addition of ^-OH to each end of the carbonyl system, has been shown (24, 74) to add 1,2 to the twinned system rather than 1,4.



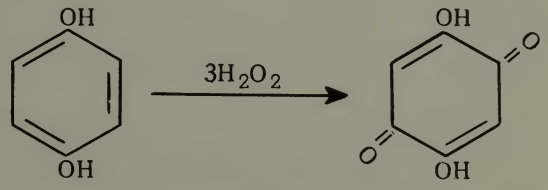
Highly-hindered materials like mesitylbenzylglyoxal – which resist reagents adding 1,2 – are cleaved easily by the hydroperoxide anion.

Typical Procedure for Ketone Cleavage (23)

Add an excess of 15% hydrogen peroxide to a methyl alcoholic solution of mesitylbenzylglyoxal (1 g.). Make the solution alkaline with sodium hydroxide and warm on a water-bath until the yellow color disappears. Cool and extract with ether. The ether extract will contain no unchanged material. A mixture of phenylacetic and trimethylbenzoic acids is obtained quantitatively by acidifying the aqueous layer.

Quinone Formation

In a few instances, aromatic rings have been converted (62, 251) to quinones with alkaline peroxide. The reaction is not general and an excess of alkali is required. 2,5-Dihydroxyquinone (80% yield) has been obtained in 65% aqueous caustic by the oxidation of hydroquinone.



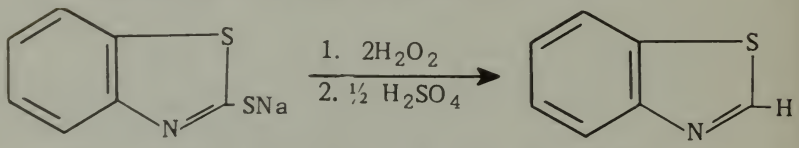
The product is not formed in solutions containing less than 15% alkali.

Organic Sulfur Oxidation

Mercaptans, such as thiophenol and octyl mercaptan, are oxidized quantitatively to disulfides by aqueous alkaline hydrogen peroxide. The mercaptans are usually dissolved in alkali, forming mercaptide salt solutions to which hydrogen peroxide is added (110, 206). Dilute sulfuric acid may be added with

the peroxide to avoid cleavage of the disulfide product by strong alkali. The reduction of alkalinity also helps to precipitate the product.

The action of excess hydrogen peroxide on the 2-mercaptide of benzothiazole causes (394) complete desulfurization to form the thiazole derivative.

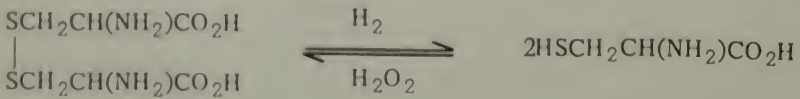


The reaction depends on the use of a 2:1 molar ratio of hydrogen peroxide to mercaptan to produce the sulfinic acid derivative. The sulfinic acid liberates sulfur dioxide upon the addition of sulfuric acid. The peroxide desulfurization procedure permits the manufacture of benzothiazole from relatively low-cost material. Benzothiazole is usually prepared from expensive 2-aminothiophenol and formic acid. Other oxidizing agents such as sodium hypochlorite convert 2-mercaptobenzothiazole to the disulfide.

Hydrogen peroxide has also converted (275) 2-mercaptobenzothiazole to 2-hydroxybenzothiazole under more alkaline conditions.

Care should be taken in handling mercaptans and thiophenols. Direct contact with these toxic materials may produce skin irritations and such unpleasant symptoms as drooping eyelids and headaches (200).

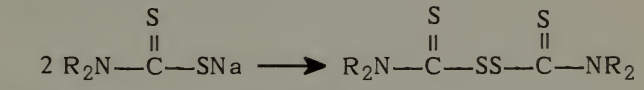
The principle of sulfhydryl oxidation is employed commercially in hair waving compositions. Waving lotions usually contain a reducing agent to convert the disulfide bonds of the hair keratin to sulfhydryl groups.



cystine *cysteine*

The reduction is carried out while the hair is wound on curlers resulting in detensioning of the hair. The disulfide linkages are reformed by the action of neutralizer solutions containing alkaline hydrogen peroxide or sodium perborate. The rebuilding of the cystine molecules by oxidation gives the hair a positive curled set.

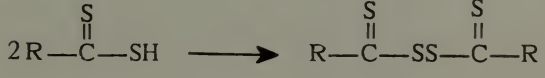
Dithiocarbamic acid salts – prepared by reacting carbon disulfide, primary or secondary amines, and alkali – are converted to disulfides by hydrogen peroxide (200).



Thiuram disulfides, as these materials are called, are important as rubber accelerators and fungicides (152). The tetramethyl- and tetraethyl-derivatives marketed as Thiuram M and Thiuram E are used to improve the vulcanization of latex and natural or synthetic rubbers. "Tersan"* 75 fungicide containing tetramethylthiuram disulfide as the active ingredient is useful for treating turf and vegetables. The literature also refers to these disulfides as suggested components of seed disinfectants, insecticides, rubber plasticizers, and polymerization catalysts.

Thiuram monosulfides, also effective as rubber accelerators, have been prepared (388) by oxidizing a mixture of sodium dialkyl dithiocarbamate and sodium cyanide with ammonium persulfate or hydrogen peroxide. The monosulfide, known as "Thionex"* tetramethyl thiuram monosulfide, can also be prepared from tetramethyl thiuram disulfide ("Tuads") by the action of sodium cyanide.

Dithio acids are also oxidized by hydrogen peroxide to form thioacyl disulfides (200).



Benzoyl persulfide has been prepared (381) by reacting benzoyl chloride and sodium hydrosulfide, followed by oxidation with hydrogen peroxide.

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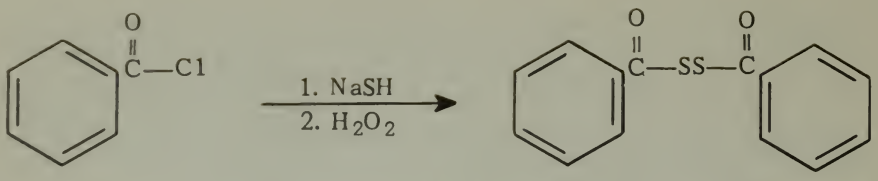
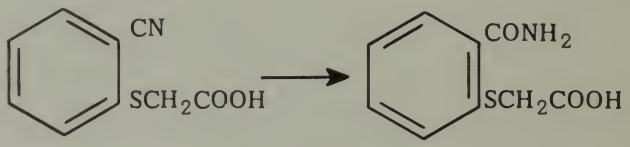


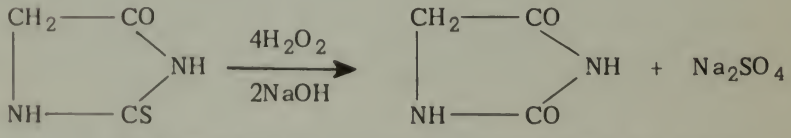
The persulfide has been used to relieve itching of the skin caused by a variety of skin conditions.

Sulfide linkages are ordinarily unreactive to the hydroperoxide anion (231). Alkaline hydrogen peroxide, therefore, converts cyano-arylthioglycolic acids to the acid amide leaving the sulfide function intact.



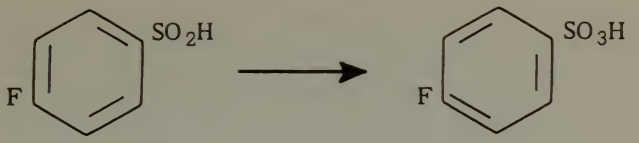
Peracids, of course, oxidize sulfides to sulfoxides and sulfones and are unreactive toward nitrile groups.

Organosulfur compounds containing thioketone linkages or sulfhydryl groups capable of tautomeric rearrangements readily undergo replacement of the sulfur atom by oxygen in alkaline hydrogen peroxide solutions (273, 274, 275). Thiohydantoin, for example, is converted in good yields to hydantoin (271).



The presence of alkali is required (272) for the replacement of sulfur since hydrogen peroxide in acidic or neutral media produces disulfides, sulfinic acids, and other sulfur derivatives. The reaction is useful for determining organic sulfur, especially non-ionizable sulfur (271).

Sulfinic acids, which can be prepared by oxidizing mercaptans and thioureas with neutral hydrogen peroxide, have been oxidized (215) further to sulfonic acids by alkaline peroxide.



p-Fluorophenylsulfinic acid derivatives, like the benzyl-ψ-thiourea salt of the sulfonic acid, have been tested as chemotherapeutic agents in treating pneumonia.

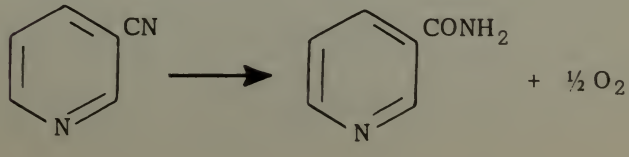
Typical Procedure for Oxidation of Organic Sulfur (110)

Suspend 1-mercaptobenzothiazole (25 g.) in water (200 ml.), and then add sodium hydroxide until the mercaptobenzothiazole goes into solution as the sodium salt. Heat the mixture to 95°C. and add 30% hydrogen peroxide solution (9.5 g.) acidified with concentrated sulfuric acid (4 ml.). Maintain, agitation throughout the reaction. Dibenzothiazyl disulfide precipitates immediately. Filter the product, wash several times, and dry.

Partial Hydrolysis of Nitriles

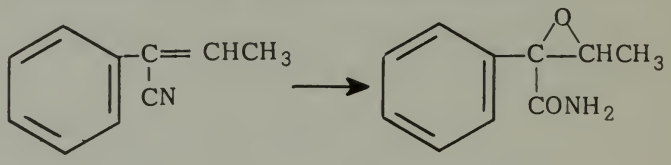
Nitriles are hydrolyzed to amides by alkaline hydrogen peroxide. The conversion of benzonitrile to benzamide involves (486) the hydroperoxide anion (^-OOH) in the rate-determining step. The rate of hydrolysis of benzonitrile and derivatives by the hydroperoxide ion in 50% acetone is apparently 10^4 times faster than that of the hydroxyl ion. The conversion of nitriles to amides proceeds satisfactorily with aromatic nitriles, especially those lacking ortho-substituents. Alkyl cyanides do not always give good results (133).

The reaction is useful for the partial hydrolysis of such materials as nicotinonitrile (116), o-tolunitrile (352), and others.



Nitriles which are difficult to hydrolyze completely to the carboxylic acid by ordinary procedures also undergo partial hydrolysis with difficulty. Thus o-substituted aromatic nitriles which are more difficult to hydrolyze require 30% and higher concentrations of peroxide for good results. Practically quantitative yields of amides have been obtained otherwise by use of 6%-12% hydrogen peroxide solutions.

Partial hydrolysis and epoxidation proceed simultaneously with α,β-ethylenic nitriles (345).



In the above reaction, α-phenyl-β-methylglycidamide is produced in 92% yields by use of hydrogen peroxide and sodium carbonate in aqueous acetone. The formation of oxido amides apparently requires olefinic unsaturation alpha,beta to the nitrile group. Allyl cyanide, on the other hand, gives only vinyl acetamide in 80% yields.

$$CH_2{=}CHCH_2CN \longrightarrow CH_2{=}CHCH_2CONH_2$$

Adiponitrile and sebaconitrile have been hydrolyzed to ω-cyanovaleramide and ω-cyanopelargonamide in low yields, 31% and 6% respectively (494). Only one of the nitrile groups responds to this treatment.

Where amides are required to be prepared from nitriles in high purity and good yields, the use of alkaline peroxide offers a superior method. Amides can also be prepared and isolated by the use of sulfuric acid monohydrate and, in some cases, aqueous alkaline solutions. These methods, however, often produce byproducts as a result of complete hydrolysis of the nitrile or complete hydrolysis and decarboxylation. Byproducts are objectionable in the preparation of amides intended for medicinal purposes.

Typical Procedure for Nitrile Hydrolysis (116)

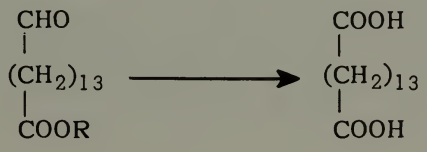
Weigh dried nicotinonitrile (2 g.) into a 200 ml. round-bottom flask, and add ethyl alcohol (10 ml.) and 30% hydrogen peroxide (7.5 g.) in the molar

ratio of 3.5:1 of hydrogen peroxide to nicotinonitrile. Chill the flask containing the mixture in an ice bath, and add 6.3N sodium hydroxide (0.95 ml.) slowly so that the temperature does not exceed 50°C. When the exotherm subsides, heat the reaction mixture at 50°C. for 6 hours. Neutralize the mixture immediately with 5% sulfuric acid and evaporate the solvent under reduced pressure. Extract the dry residue 15 times with 10 ml. portions of hot ethyl acetate. Dry the product obtained by evaporating ethyl acetate. Nicotinamide (87.4% yield) is obtained in 98.75% purity.

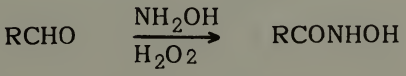
Oxidation of Aldehydes

Aliphatic and aromatic aldehydes alike are reactive to alkaline hydrogen peroxide forming unstable peroxides as primary products. Carboxylic acids are almost always the final products of the oxidation of aliphatic aldehydes. Aromatic aldehydes are usually converted to phenols.

Pentadecanedioic acid, useful in the synthesis of the musk cyclopentadecanone, is prepared by treating alkyl aldehydopentadecanoate with an aqueous alkaline solution of hydrogen peroxide (292). The ester is saponified during reaction to give the dicarboxylic acid salt.



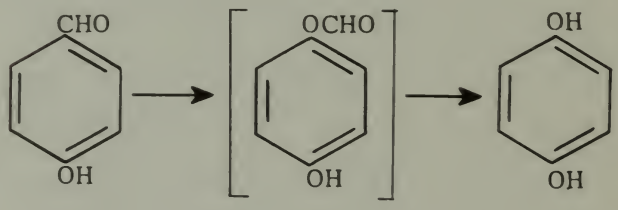
Water-soluble aldehydes mixed with alkaline solutions of hydroxylamine form (354) hydroxamic acids with the addition of two equivalents of hydrogen peroxide.



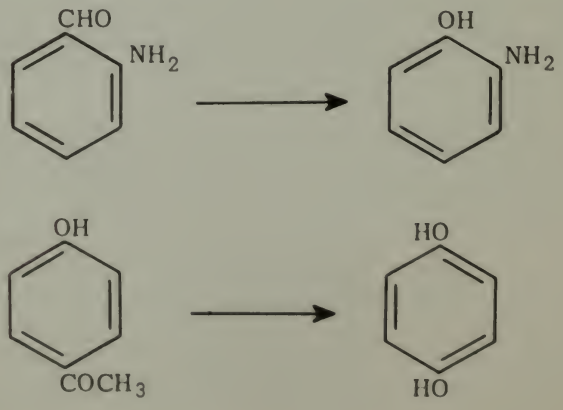
The hydroxamic acids may be formed by the action of hydrogen peroxide on an intermediate oxime. Another interpretation (4) of this reaction, however, involves the oxidation of hydroxylamine to form a nitrosyl derivative which reacts with the aldehyde. Insoluble aldehydes like butyraldehyde and aromatic aldehydes do not undergo the reaction.

A method generally applicable to the preparation of catechols is the oxidation of o-hydroxybenzaldehydes with alkaline hydrogen peroxide. This procedure (124, 125) usually gives satisfactory yields unless the aldehyde group is hindered by large ortho substituents.

p-Phenolic aldehydes are oxidized smoothly to dihydroxy derivatives at room temperature using concentrations less than 3% hydrogen peroxide. Intermediate formyl groups are rapidly hydrolyzed.

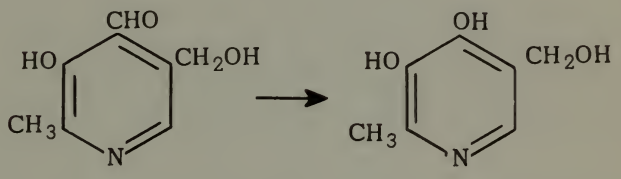


The reaction has been termed the Dakin reaction and has been extended to include the oxidation of o- and p-aminobenzaldehydes (16) and ketophenols (87).



Evidence for the formation of an intermediate peroxide rearranging to the acyl derivative has been obtained (466).

The Dakin reaction has been used (232) to prepare pyridine derivatives having vitamin B_6 activity.



Such derivatives as 2-methyl-3,4-dihydroxy-5-hydroxymethylpyridine in small quantities with ferric salts give very deep colors varying from red to purple. These colored compounds may be used in the manufacture of inks, dyes, or as a means of determining traces of ferric iron in solution.

The Dakin reaction is applicable to almost all hydroxy aldehydes or ketones in which the hydroxyl and carbonyl groups occupy ortho or para positions relative to each other. When applied to substances sparingly soluble in aqueous alkali, the reaction is best carried out by adding hydrogen peroxide and concentrated alkali to a solution of the material in pyridine (21). Certain derivatives of hydrogen peroxide such as persulfates or sodium peroxide may also be employed, but their use is far less convenient.

Typical Procedure for Aldehyde Oxidation (232)

Dissolve 5 grams of 2-methyl-3-hydroxy-4-formyl-5-hydroxymethylpyridine hydrochloride in water (15 ml.). Cool the solution in an ice bath and add sufficient 6N sodium hydroxide to adjust the solution to pH 10. Remove the bright yellow mixture thus formed from the ice bath and add hydrogen peroxide (30%) dropwise. The mixture will become colorless after the addition of about 5 ml. of peroxide. Cool the mixture in an ice bath, and acidify to pH 5 with hydrochloric acid. Crystals of 2-methyl-3,4-dihydroxy-5-hydroxymethylpyridine separate from solution.

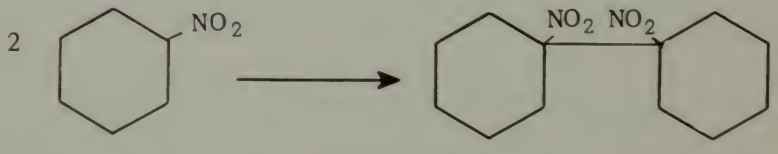
Purification of Organic Materials

Dilute alkaline hydrogen peroxide solutions are especially suited to the improvement and purification of organic matter on a commercial scale. The alkaline reagent is more easily handled than peracids, for example, and does not require recovery of organic acids and may be prepared as needed, eliminating special storage systems.

Among the many materials which have been improved by peroxide treatments are tobacco (221), folic acid (475), glutamic acid (144), and fatty acid esters (26). Synthetic folic acid, not easily separated from contaminants, has been obtained in 95% purity suitable for pharmaceutical uses by treatment with alkaline hydrogen peroxide. High purity monosodium glutamate has been prepared by adding hydrogen peroxide to the alkaline hydrolysis reaction of glutamic mother substances including beet molasses residues and desaccharified beet molasses. Alkaline hydrogen peroxide has also been used successfully in the refining of crude fatty acid esters intended for industrial or edible purposes. The peroxide method supplants or supplements bleaching treatments by adsorbing clays or other chemical agents.

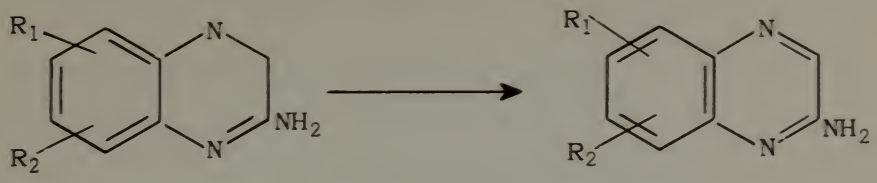
Miscellaneous Reactions

Aliphatic and alicyclic nitro compounds have been condensed by alkaline peroxide producing dinitro hydrocarbons (111). Formation of the dinitro derivatives is favored by use of an aqueous medium which causes precipitation of the product before other polynitro compounds are formed.



Polynitro derivatives predominate when organic solvents and vigorous reaction conditions are employed.

At least one example (366) of heterocyclic ring dehydrogenation by hydrogen peroxide appears in the literature. 2-Amino-3,4-dihydroquinoxalines are converted under alkaline conditions to 2-aminoquinoxaline compounds in 50% yields.



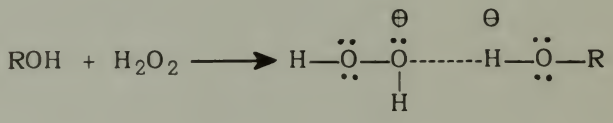
Yields are increased to 60% by hydrogen peroxide activated with ferrous iron; 80% by acidic hydrogen peroxide. The quinoxalines are important intermediates in the manufacture of sulfaquinoxalines which are used as bacteriostatic agents in veterinary medicine.

Cellulosic materials are partially degraded by alkaline hydrogen peroxide to form solutions or dispersions of definite viscosity which form coherent films upon precipitation. Use of these solutions is made in treating and sizing textiles and paper. The degradation is carried out (77, 463) by dissolving cellulose in alkali solution to form alkali cellulose and adding hydrogen peroxide. The reaction is conducted under carefully controlled conditions to produce solutions of proper viscosity. The viscosity of carboxyalkyl cellulose ether solutions suitable for industrial applications is also regulated (278) by the use of alkaline hydrogen peroxide under metal activation. Other methods, not involving hydrogen peroxide, for degrading cellulose tend to produce excessive degradation. The products formed are incapable of forming coherent films which do not disintegrate in alkaline coagulating baths.

Oxidized starches have been prepared by treating a slightly alkaline suspension of starch and water with hydrogen peroxide and heating to a temperature below the gelatinization point. Because of the discontinuities introduced into the linear molecule by oxidation, the starch molecules resist association into micellar bundles. Thus pastes of oxidized starches are clearer, freer of dissolved solids, and more stable against gelling than thin-boiling starches prepared by acid treatment. Oxidized starches are useful for textile warp sizing, textile finishing, and the manufacture of clay-coated paper.

HYROGEN PEROXIDE IN SOLVENT AND WEAK ACID SYSTEMS

Organic oxidations with hydrogen peroxide have been performed in alcohols, nitriles, acetone, pyridine, and ethers. The use of organic solvents tends to inhibit decomposition of hydrogen peroxide by metals although the stabilizing action of the solvents varies with the metals involved. A kinetic study (356) of the oxidation of sulfides to sulfoxides indicates that reaction is promoted by solvents capable of hydrogen bonding with hydrogen peroxide. The effect of solvation by alcohol, for example, is apparently to render the peroxide molecule electrophilic, thereby increasing reaction with nucleophilic functional groups.

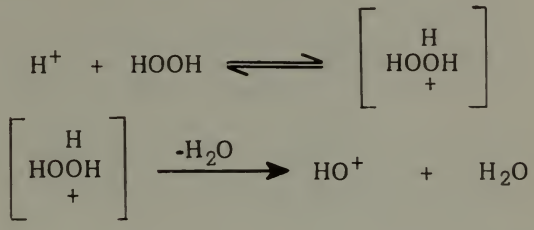


The rate of oxidation of sulfides seems to be independent of the dielectric constants of the solvents employed, however.

Certain reactions of hydrogen peroxide require establishing essentially anhydrous conditions. Such anhydrous hydrogen peroxide-ether reagents may be prepared (430) by extracting aqueous hydrogen peroxide solutions with ether, drying the ether layer over anhydrous sodium sulfate, and removing excess ether in vacuo until the solution contains 6%-12% hydrogen peroxide. The use of hydrogen peroxide-ether reagent to oxidize such molecules as aldehydes, however, may result in the formation of dangerous organic peroxides. The quantity of ether employed in these reactions is usually sufficient to produce dilute, and therefore presumably safe, solutions of the organic peroxides. Organic peroxides, however, are often entrained to the upper sides of reaction flasks by the highly volatile solvent to be deposited in a concentrated and hazardous form.

Many reactions of hydrogen peroxide are acid-catalyzed. Consequently, specific rate constants for the oxidation of sulfides in alcohol increase (356) linearly with the addition of sulfuric acid. Hydrogen peroxide, itself, is a weak acid – somewhat weaker than phenol and hydrogen cyanide. A

suitable interpretation for the activation of hydrogen peroxide by dilute acids is lacking although the formation of positively charged hydroxyl ions (^{+}OH) has been suggested (137, 392).

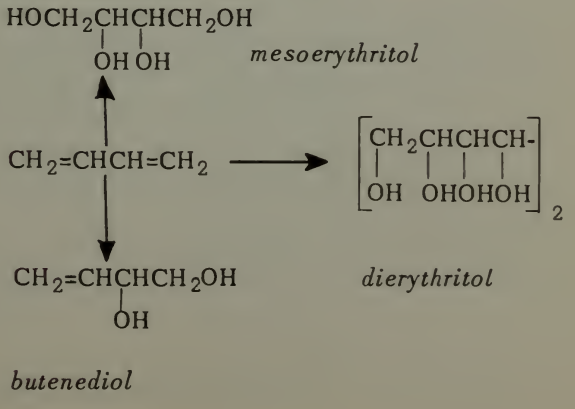


The mechanism may not apply (413) under conditions for reactions catalyzed by dilute acids.

The reactions of hydrogen peroxide in organic solvent and weak acid systems are summarized in the following paragraphs.

Hydroxylation

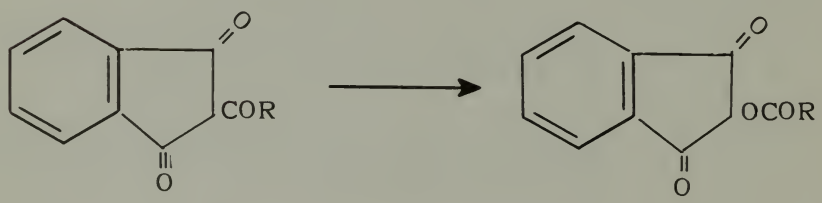
Acid or neutral hydrogen peroxide is not as effective as are peracids and metal-activated hydrogen peroxide in hydroxylation. Acid and neutral peroxides however, have been used to advantage in a few instances. Hydrogen peroxide in the presence of small amounts of lactic, tartaric, or citric acids has been employed (252) in the hydroxylation of soybean lecithin. Hydrogen peroxide, methylformate, and butadiene – heated in a sealed tube at 50°C. – produce a hydroxylated fraction consisting of unchanged butadiene (49%), mesoerythritol (11%), dierythritol (11%), and 3-butene-1,2-diol (29%).



A few other examples of such hydroxylations are described in the literature (198, 213).

Oxidative Cleavage – Ketones

Ketones and hydrogen peroxide generally react in inert solvents or in the presence of dilute acid catalysts to form organic peroxides. These reactions are discussed in detail in the section on *Preparation of Organic Peroxides.* Hydrogen peroxide (20%) kept in ether at room temperature for 21 days converts (217) 1,3-diketo-2-acetylindan to 1,3-diketo- 2-acetoxyindan.



A specific oxidizing agent for ketones has been prepared (238) by dissolving 28% aqueous hydrogen peroxide in anhydrous hydrogen fluoride. This reagent transforms 2-octanone to hexylacetate and cyclohexanone to ϵ-caprolactone. The reaction is probably more like that of hydrogen peroxide in acetic acid than like that of peroxide in inert solvents. The formation of esters from ketones is better effected by organic peracids or Caro's acid.

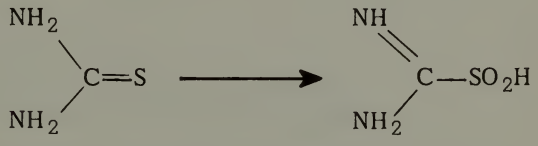
Organic Sulfur Oxidation

Hydrogen peroxide in inert solvent or aqueous solutions was first investigated (192) for oxidizing sulfides to sulfoxides because of deficiencies of the common oxidizing agent of that period, nitric acid. The action (343) of nitric acid destroyed part of the sulfide and nitrated aromatic rings producing objectionable byproducts. The reaction with hydrogen peroxide proceeds at room temperature and does not produce degradation products or significant amounts of sulfones.

thiodiglycolic acid *thiodiglycolic acid sulfoxide*

The rate of oxidation of disulfide acids (e.g. dithiodiacetic acid) by peroxide in dioxane has been found (434) to be accelerated by the presence of water. The addition of a small amount of sulfuric acid has the same effect as increasing reaction temperature by 10°C. Diresorcyl sulfoxide prepared (113) with aqueous hydrogen peroxide is used in diazo printing processes. Organic sulfoxides and disulfoxides are excellent defoliants (203).

Formamidine sulfinic acid (FSA) and derivatives have been prepared in a variety of ways involving hydrogen peroxide. The methods include the addition (25, 464) of powdered thiourea to aqueous hydrogen peroxide and the reaction (218) of aqueous thiourea and hydrogen peroxide.

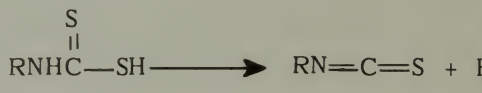


Walker (471) has prepared FSA by reacting ammonium thiocyanate melt (containing thiourea) and aqueous hydrogen peroxide. FSA is a useful reducing agent for vat dyes, water-dispersible colors, and various organic functional groups (205). It reduces nitro, azoxy, azo, and hydrazo groups to amines and quinones to hydroquinones. Ketones and α-diketones are unreactive to formamidine sulfinic acid. Formamidine sulfinic acid requires (96) an alkaline environment to exercise fully its reducing properties for textile printing. In acetic acid solutions, FSA develops reducing powers only at 100°C. in the presence of moist saturated steam.

The reaction of hydrogen peroxide and substituted thiourea in dioxane leads (449) to aminoiminomethanesulfinic acids useful as stabilizers for solutions of sympathomimetic drugs.

Mercaptans (110) and dithio carbamic acids (2) have been oxidized to disulfides by hydrogen peroxide in alcohol and dilute aqueous mineral acid solutions. The use of aqueous acids apparently is suitable for the preparation of tetraalkylthiuram disulfides.

Oxidation of the alkali salts of monoalkyldithiocarbamic acids to form monoalkylthiuram disulfides, however, – as described in the section on *Alkaline Hydrogen Peroxide Systems* – tends to reform the free dithiocarbamic acid which is converted to mustard oil compounds.



Mustard oil formation is eliminated (199) by oxidizing monoalkyl ammonium salts of the dithiocarbamic acid in acidic hydrogen peroxide.

Disulfides such as the dibenzothiazyl and the thiuram disulfides are used as rubber accelerators.

Typical Procedure for Organic Sulfur Oxidation (471)

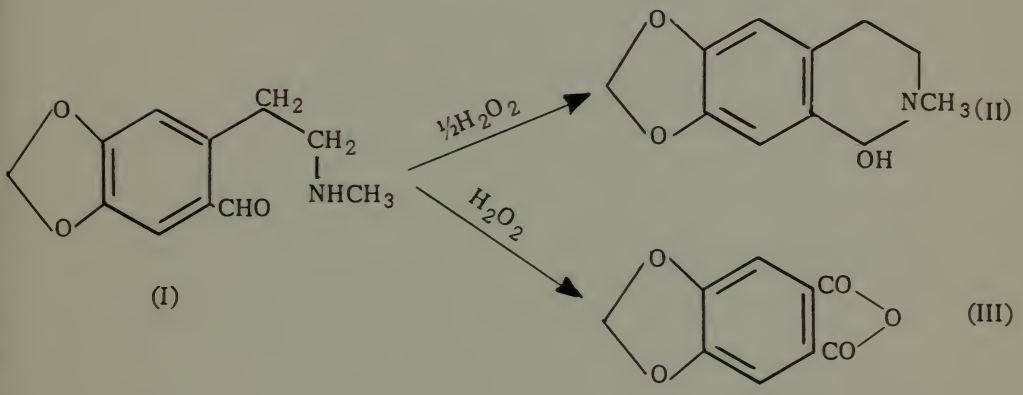
Prepare a melt containing equilibrium amounts of ammonium thiocyanate and thiourea by heating solid ammonium thiocyanate at 170°C. for one hour. Allow the melt to solidify. Dissolve 30 g. of the equilibrium melt in 150 g. of water and add 26 g. of 27.6% hydrogen peroxide. Control temperature during reaction so that it does not exceed 20°C. Formamidine sulfinic acid (82% yield) is obtained by crystallization.

Organic Nitrogen Oxidation

The oxidation of amines, azo, azoxy, and nitroso compounds is most conveniently carried out by use of mixtures of hydrogen peroxide and organic acids. The use of these mixtures to effect nitrogen oxidation has been discussed under *The Peracid Systems.* Dilute aqueous hydrogen peroxide, however, has been used (145, 314) to prepare amine oxides and hydroxylamines.

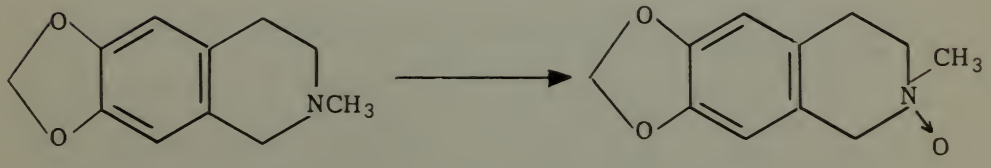
The oxidation of secondary amines to di-N-substituted hydroxylamines with 6% hydrogen peroxide has been most successful (145).

Hydrastinine (I), obtained by the oxidative hydrolysis of the alkaloid hydrastine, reacts (371) with 30% hydrogen peroxide in acetone. The products are respectively dehydrohydrastinine (II) and hydrastinic anhydride (III) depending upon the quantities of peroxide used.



(I) (II) (III)

Hydrastinine exists in three tautomeric forms (201); the imino aldehyde (I), the pseudobase (II), and the quaternary base [–CH=N(OH)CH3]. Hydrohydrastinine (IV) is converted by hydrogen peroxide to the N-oxide (V).



(IV) (V)

Hydrastinine has therapeutic value in reducing uterine hemorrhage.

Typical Procedure for Organic Nitrogen Oxidation (145)

Add 3% hydrogen peroxide (60 ml.) – previously freed from sulfuric acid by shaking with barium carbonate – to an aqueous solution containing 3 grams of trimethylamine. After allowing the mixture to stand for 24 hours at room temperature, concentrate the solution to 20 ml. *in vacuo*. Acidify the solution with a slight excess of hydrochloric acid and reduce solution volume further to 5 ml. Trimethylamine oxide hydrochloride is obtained by crystallization.

Hydrogen Peroxide – Amide Complexes

Hydrogen peroxide replaces partially, or wholly, the water of crystallization held by certain organic compounds with weak base properties. The structure of the organic compounds with which hydrogen peroxide complexes generally includes amide linkages. The peroxide complexes formed have varying degrees of stability toward loss of active oxygen. All of the peroxide complexes have, more or less, the property of releasing hydrogen peroxide gradually.

The best known of these materials are the urea peroxides ("hyperols" or "percarbamides"). Urea has been combined (22) with one to four moles of hydrogen peroxide. The peroxide-rich complexes of urea are less stable but have not been detonated. Urea peroxides are obtained (22, 254, 342) by crystallization from a mixture of aqueous hydrogen peroxide and urea.

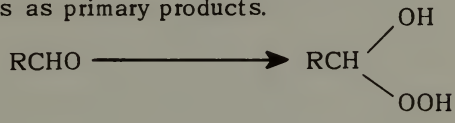
$$NH_2CONH_2 \longrightarrow NH_2CONH_2 \cdot xH_2O_2$$

Cyanoguanidine does not form peroxide complexes, indicating that an imino-amino linkage is not effective. Urea-type compounds forming peroxide complexes include the methylolureas (254), acetamide (22), diacetylhydrazine (285), and malonic and succinic acid azides (285).

A few compounds lacking amide linkages also form hydrogen peroxide complexes. These include sodium formate, sodium α-chloropropionate, glycine, quinine sulfate, and urotropine (285).

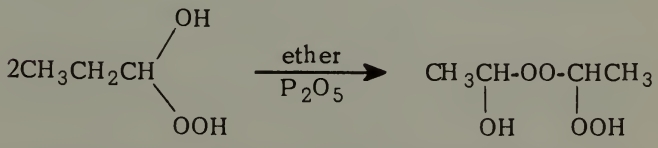
Oxidation of Aldehydes

Whether reacting with peracids, alkaline peroxide, or other activated forms of hydrogen peroxide, aldehydes are believed to produce hydroxy hydroperoxides as primary products.



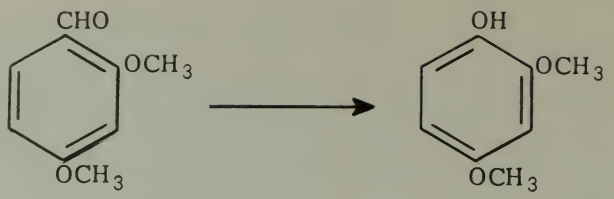
Like gem-diols, these peroxides tend to rearrange or combine with molecules of their kind to form more stable configurations. In peracid and alkaline peroxide systems, the aldehyde peroxides tend to rearrange to carboxylic acids or alcohols. In anhydrous systems, especially, the intermediate peroxides are stable or may self-condense to form cyclic or disubstituted peroxides. Hydroxy hydroperoxides are often stable in ether solution but decompose upon removal of the solvent. Therefore, many reactions of aldehydes and hydrogen peroxide in inert solvent systems and occasionally in dilute acid are hazardous.

Self-condensation of the primary hydroxy hydroperoxide of propionaldehyde produces (387) a product richer in active oxygen.



Further condensations of the hydroxy hydroperoxy dialkyl peroxide may produce the cyclic tripropylidene triperoxide which is extremely explosible.

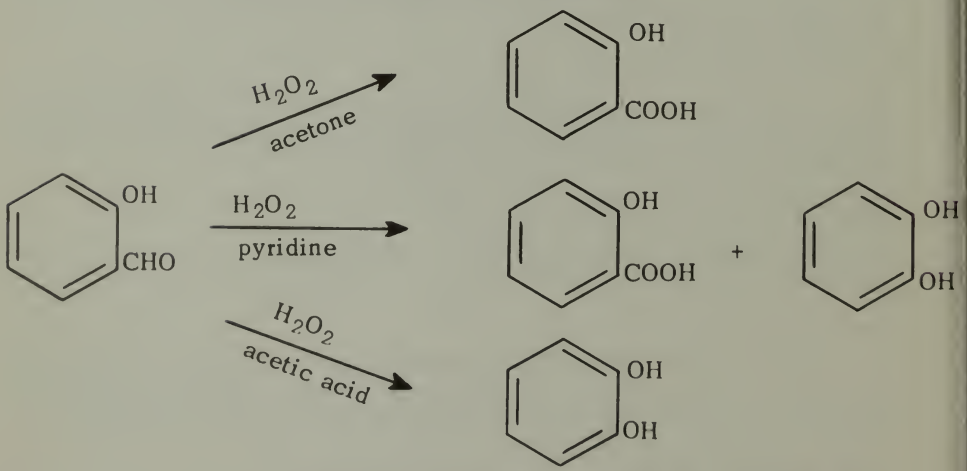
Alkoxy-substituted benzaldehydes produce (430) alkoxy phenols upon reaction with hydrogen peroxide-ether reagent. Vigorous reaction ensues upon evaporation of the ether solvent, probably indicating rearrangement of the primary peroxide product.



Small amounts of carboxylic acids are formed as the position and number of the alkoxy substituents are varied. In the oxidation of benzaldehyde, having no alkoxy substituents, the yield of carboxylic acid considerably exceeds the yield of phenol.

Hydrogen peroxide in acetone converts (239) phenolic aldehydes quantitatively to salicylic acid. Hydrogen peroxide-pyridine produces 20% pyrocatechol and 75% salicylic acid.

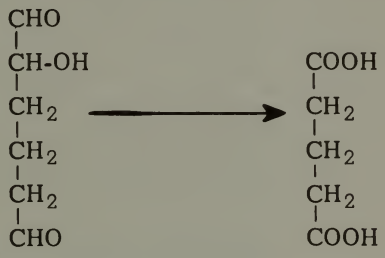
Peracids and alkaline hydrogen peroxide convert phenolic aldehydes to catechols.



Anhydrous solutions of hydrogen peroxide convert (466) o-aminobenzaldehyde to anthranil.

Alkaline peroxide, on the other hand, forms o-aminophenol.

Oxidation of aldehydes in aqueous acid medium ordinarily produces (40, 362) the corresponding carboxylic acid. Thus propionaldehyde gives propionic acid; benzaldehyde, benzoic acid; and glycolaldehyde, glycolic acid which may be oxidized further. A convenient method of preparing (485) glutaric acid consists of adding hydrogen peroxide to an aqueous solution of α-hydroxyadipaldehyde at 80°C.



The starting aldehyde is obtained by hydrolyzing 3,4-dihydro-1,2-pyran-2-carboxyaldehyde. Pyridine-3- and pyridine-4-aldehyde are oxidized smoothly to form (277) nicotinic and isonicotinic acids. Pyridine-3-aldehyde also responds to air oxidation; pyridine-4-aldehyde, only after several weeks. Pantothenic acid, a vitamin B substance, is formed (197) in the oxidation of the aldehyde.

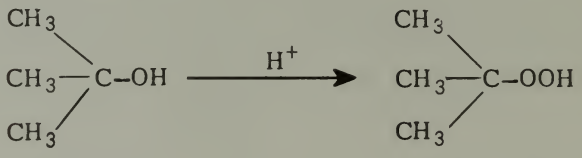
Typical Procedure for Oxidation of Aldehydes (485)

Prepare α-hydroxyadipaldehyde by hydrolyzing 267 g. of 3,4-dihydro-1,2-pyran-2-carboxaldehyde in 560 g. of 0.0216N sulfuric acid (at room temperature for 2½ hours). Neutralize the acid with excess calcium carbonate and filter. The filtrate contains α-hydroxyadipaldehyde (90% yield).

To the filtrate add 840 g. of 30% hydrogen peroxide in 6 portions at regular intervals over a 48-hour period. Allow the temperature to rise to 80°C. during the addition of hydrogen peroxide. After addition of peroxide has been completed, maintain the reaction mixture at 80°C. for 8 hours longer and evaporate the solution *in vacuo*. Glutaric acid (95% purity) is obtained in 89% yield (313 g.) as a white solid.

Oxidation of Alcohols

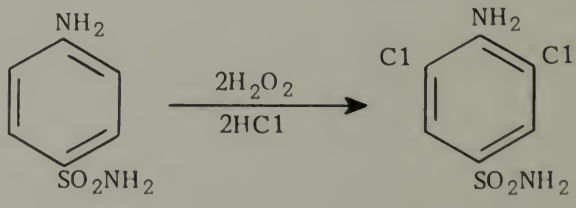
The oxidation of alcohols by hydrogen peroxide in inert solvents, or under catalysis by acids, usually produces organic peroxides. Criegee and Dietrich (120), for example, prepared t-butylhydroperoxide by reacting 78%-90% hydrogen peroxide and t-butyl alcohol at $0^{\circ}C$.



Primary alcohols are slow to react, but the reaction of secondary and tertiary alcohols proceeds at a practical rate. Di-t-butyl peroxide is obtained by increasing the ratio of alcohol to hydrogen peroxide. Peroxide-alcohol mixtures have exploded (120) resulting in critical injuries to investigators.

Halogenation of Aromatic Rings

Aromatic ethers are rapidly halogenated (46, 253) when mixed with halogen acid and treated with hydrogen peroxide. Chloro-, bromo-, and iodo-derivatives have all been prepared in yields often exceeding 85%. The reaction is by no means restricted to ethers, for sulfanilamide has been chlorinated and brominated (414) in this fashion.



2,6-Dichloroaniline, containing positive halogen atoms (86), is prepared by desulfonamidation of 3,5-dichlorosulfanilamide.

Typical Procedure for Halogenating Aromatic Rings (414)

Place 50 g. (0.29 mole) of sulfanilamide and 500 ml. of water in a 2-liter round-bottomed flask fitted with a mechanical stirrer and a thermometer. Add about 50 ml. of a 500-ml. portion (about 6 moles) of concentrated hydrochloric acid and stir the mixture until a clear solution results. Add the remainder of the hydrochloric acid. If necessary, heat the reaction mixture gently until a temperature of 45°C. is reached. Add 65 g. (0.58 mole) of 30% hydrogen peroxide and stir rapidly. Allow the reaction temperature to reach 60°C. and maintain at this temperature for 15 minutes by cooling. While stirring, cool the mixture to 25°-30°C. by means of an ice bath. When the mixture reaches this temperature, collect the solid product – 3,5-dichlorosulfanilamide – by filtering immediately. The yield is 45-50 g. (65%-71%).

Purification of Organic Materials

Like alkaline hydrogen peroxide, hydrogen peroxide in dilute aqueous medium is convenient for the purification of organic materials on a commercial scale. Among such uses for hydrogen peroxide are included the refining of sugar solutions (287), the depolymerizing of dextran to smaller molecules suitable for blood plasma extenders (293), the bleaching of glycerides (3), and the coagulating of latex (484). Hydrogen peroxide, decomposed by catalase, is also used (447) to provide oxygen for converting natural rubber latex to foam rubber.

METAL-ACTIVATED HYDROGEN PEROXIDE SYSTEMS

The mild oxidizing action of hydrogen peroxide is increased considerably by use of certain metallic catalysts. This observation was first made in 1894 by Fenton (164), who obtained such products as glyceraldehyde by oxidizing glycerine in the presence of the reducing substance, ferrous sulfate. The redox system Fe^{++}-Fe^{+++} employed with hydrogen peroxide has become known as Fenton's reagent. Fenton's work on alcohols has been supplemented (339) by the use of catalysts such as osmium and tungstic oxides to hydroxylate aromatic and unsaturated hydrocarbons and to effect other oxidations. Such catalysts used with hydrogen peroxide are classed as Milas' reagents which, together with Fenton's reagent, constitute the bulk of the metal-activated hydrogen peroxide systems. Hydrogen peroxide in metal-activated systems reacts as though it were dissociating into two hydroxyl radicals.

Fenton's oxidations are, in fact, believed to proceed through the intermediate formation of hydroxyl free radicals (8, 20, 27, 317).

$$Fe^{++} + H_2O_2 \longrightarrow Fe^{+++} + OH^- + \cdot OH$$

The initiation of addition polymerization by Fenton's reagent is considered evidence for the existence of hydroxyl radicals. Such polymerizations carried out simultaneously with the oxidations of certain organic substrates have shown the reactions to be competitive. Therefore, the same activated entity, the hydroxyl free radical ($\cdot OH$), is presumed to be involved in both reactions.

How ferrous and ferric ions are involved in Fenton's oxidations is not clear except that ferrous ions are believed to generate hydroxyl free radicals. There is evidence to show that ferric ion concentration has an important effect on the reaction. In Fenton's oxidation of benzene, for example, the formation of phenol at high ferric ion concentration is favored to the virtual exclusion of diphenyl formation. When fluoride or phosphate ions are used to remove ferric ions from the system by forming inactive complexes, the oxidation of benzene is inhibited (344). In the absence of conclusive evidence, ferric ions are assumed to be involved in the oxidation of the substrate free radicals ($R\bullet$) to form the expected products of Fenton's oxidation.

$$\bullet OH + RH \longrightarrow H_2O + R\bullet$$

The substrate radicals, as shown in the above equation, are formed by the action of the hydroxyl free radicals.

The Fe^{++}-Fe^{+++} system, and such other redox systems as Cu^{+}-Cu^{++}, are normally employed with hydrogen peroxide in aqueous acid medium. A small amount of sulfuric acid is added to an aqueous solution of ferrous sulfate heptahydrate so that Fenton's oxidations are carried out at pH 1-4. In less acid solution reaction efficiency is decreased, and hydrogen peroxide is catalytically decomposed.

Although other interpretations (326) have been considered, osmic acid (OsO_4) and tungstic acid (WO_3) – unlike Fenton's reagent – may involve the intermediate formation of inorganic peracids. Consequently, any of the inorganic peracid-formers take part in Milas-type oxidations. A list of such peracid-formers includes (326, 344) OsO_4, WO_3, MoO_3, SeO_2, CrO_3, V_2O_5, TiO_2, Ta_2O_5, and others. The catalysts are listed above in the order of decreasing efficiency under the same reaction conditions. Derivatives of the above catalysts, such as the phosphotungstic acids (e.g. $H_3PO_4 \bullet 12WO_3$), are also effective as catalysts for hydrogen peroxide.

Milas' reagent is prepared by dissolving the metal oxide in t-butyl or t-amyl alcohols containing the organic substrate. To this mixture is added anhydrous hydrogen peroxide in alcoholic solution. The solution is made anhydrous by salting out the alcoholic peroxide layer and drying it with anhydrous sodium sulfate. Osmium tetroxide usually requires the use of an inert solvent. Vanadium pentoxide is insoluble in the above alcohols, but the addition of alcoholic hydrogen peroxide causes (319, 456) the formation of the deep red, alcohol-soluble pervanadic acid (HVO_4). Chromic anhydride (CrO_3) is soluble in both t-butyl and t-amyl alcohols, forming a reddish solution which turns deep blue upon the addition of hydrogen peroxide. The exact composition of the blue peroxyacid thus formed is uncertain but appears to be CrO_5. Water and glacial acetic acid are also used as solvents for Milas-type oxidations, depending upon the solubilities of the organic substrates and the metal oxide catalysts.

It should be remembered that catalysts used in metal-activated hydrogen peroxide systems also catalyze active-oxygen decomposition by converting hydrogen peroxide to a less stable form. Therefore, the reaction conditions under which such systems are operated must be carefully controlled to avoid excessive decomposition. Under proper conditions for use of the Fe^{++}-Fe^{+++} system, catalysis of oxidation by hydrogen peroxide is said to be (473) 3000 times greater than that of its decomposition.

The convenience of considering the reactions of the metal-activated hydrogen peroxide systems as though proceeding through the dissociation of hydrogen peroxide into two hydroxyl radicals is apparent. This is true whether or not the reactions involve the formation of hydroxyl free radicals in Fenton's oxidations or intermediate inorganic peracids in Milas' oxidations.

Epoxidation

Recent work (423) has indicated that systems involving metal-catalyzed hydrogen peroxide can be used for epoxidation. The system is operated by dissolving the epoxidizable substance in t-butyl alcohol-water mixtures to which is added a small quantity of tungstic or molybdic acid catalyst. Excess hydrogen peroxide is then charged to the mixture held at 70°-80°C. until reaction is complete. Hydrogen peroxide used in this manner has transformed the insecticide Aldrin to the epoxy insecticide Dieldrin in 95% yields. As yet, metal-catalyzed hydrogen peroxide systems have not found wide usage in industry but offer considerable promise.

Hydroxylation of Unsaturated Compounds

The hydroxylation of unsaturated compounds is the best known reaction of metal-activated hydrogen peroxide. The compounds undergoing reaction may contain (326, 340) halogen, carboxylate, carbonyl, alcohol, and ether linkages without hindering hydroxylation. Double-bonded carbons having such electron-releasing substituents as alkyl groups, however, apparently hydroxylate at a faster rate (37, 79, 107, 319, 391).

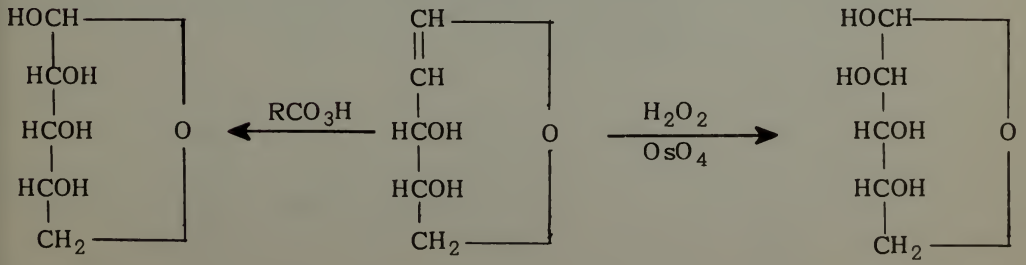
Terminal double bonds, which resist peracids, are hydroxylated (344) by metal-catalyzed hydrogen peroxide although at a slower rate than internal double bonds. In general, the Fe^{++}-Fe^{+++} system is not as efficient as Milas' catalysts in hydroxylating unsaturated hydrocarbons.

Few oxidizing agents are satisfactory in the hydroxylation of unsaturated aldehydes because they tend to oxidize the aldehyde group. Under proper conditions, hydrogen peroxide catalyzed by osmic acid hydroxylates (344, 421) acrolein at 25°-30°C. producing glyceraldehyde (80% yield).

$$CH_2{=}CHCHO \longrightarrow \underset{\underset{OH}{|}}{CH_2}\underset{\underset{OH}{|}}{CH}CHO$$

Oxidation of the aldehyde group is prevented by adding hydrogen peroxide to the reaction mixture at a rate such that osmium oxide (OsO_2) is produced and maintained in excess during hydroxylation. If required, acrolein may be oxidized (323, 504) to glycerine by use of osmic, tungstic, or molybdic catalysts at higher temperatures. Peracid systems do not hydroxylate α,β-unsaturated aldehydes effectively while alkaline peroxide produces the epoxide. Both of the latter reagents attack the aldehyde group. Hydroxylation is also effected by such reagents as chlorates. Products obtained by use of these reagents, however, are not easily isolated in sufficient purity. The chlorates have a tendency to form chlorinated byproducts, and the oxidizing agent contaminates the product as well.

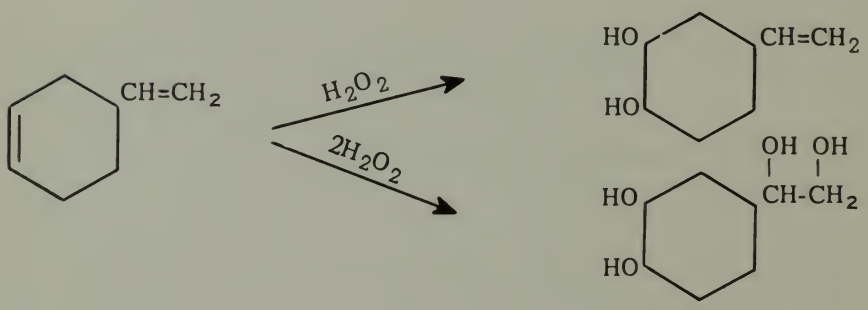
Hydrogen peroxide, catalyzed by osmic acid in t-butanol, converts the glucal d-arabinal to d-arabinose, which is difficult to obtain and rarely occurs in nature. Perbenzoic acid oxidizes d-arabinal to the more abundant d-ribose (34, 35, 229, 230).



d-ribose *d-arabinal* *d-arabinose*

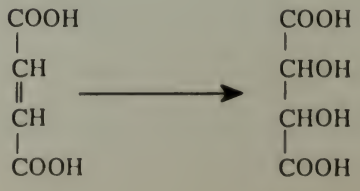
The reactions demonstrate how a choice of the proper active-oxygen system may be made to achieve desired results. The use of hydrogen peroxide thus provides a method for converting aldose sugars into their epimers.

A consideration of experiments (344) on vinyl cyclohexene points up the relative ease with which terminal and isolated unsaturation is hydroxylated. Using one mole of hydrogen peroxide results in the complete hydroxylation of the internal double bond while the terminal unsaturation remains unaffected. All available unsaturation reacts upon use of two equivalents of peroxide.



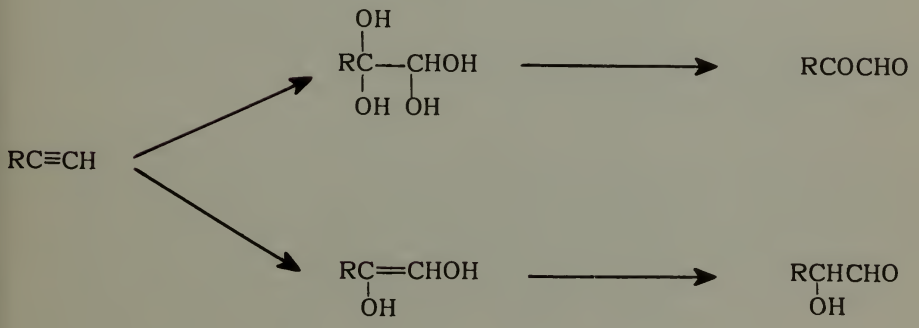
A choice of catalyst often affects the configuration of the diol formed. Thus, the use of tungstic acid with hydrogen peroxide at 50°C. produces the trans-diol of cyclohexene in 77% yield. The cis-diol is formed in 47% yield upon use of osmic acid in t-butanol at 20°C.

A possible commercial process for manufacturing tartaric acid consists (107) of reacting an aqueous mixture containing a 1.5:1 ratio of maleic acid and hydrogen peroxide with 0.5% tungstic acid at 80°-100°C.

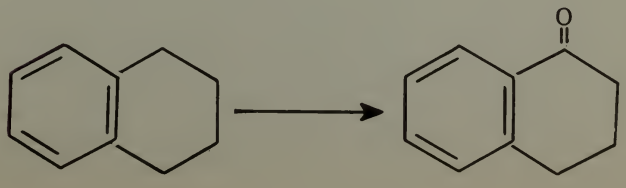


The racemic mixture is formed in 95% yields, involving trans-addition to the double bond. Milas and Sussman (339) obtained meso-tartaric acid and *dl*-tartaric from maleic and fumaric acids respectively by use of osmic acid-catalyzed hydrogen peroxide. Meso-tartaric acid is also prepared in the permanganate oxidation of maleic acid through cis-addition. Tartaric acid is usually obtained from argol or wine lees formed in the manufacture of wine. Large quantities of tartaric acid are used in the food and pharmaceutical industries.

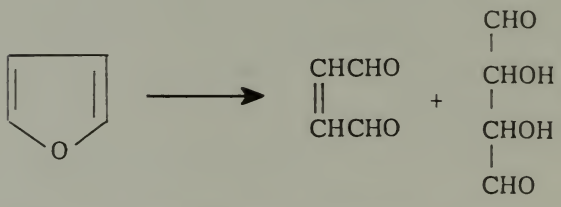
A variety of other products has been obtained by reaction of unsaturated hydrocarbons and metal-catalyzed hydrogen peroxide. The products formed depend upon the structure of the hydrocarbon and the reaction conditions, employed. The metal-catalyzed system is not limited solely to olefinic linkages. Acetylenes are also oxidized (323) to form keto acids, glyoxals, glycolic acids, and glycolaldehydes.



Peroxy acids of vanadium catalyze (458) the oxidation of cycloolefins and hydroaromatic compounds by hydrogen peroxide. The products are usually ketones. α-Tetralone, for example, is formed in 50% yields by the oxidation of tetralin.



Aldehydes and ketones are occasionally obtained as products of hydroxylation (109) indicating that intermediate vicinal diols have undergone 1,4-diradical cleavage under the influence of the metal-catalyzed hydrogen peroxide. The hydroxylation of furan by OsO_4 catalysis in methanol produces (109) aldehydomaleic and aldehydotartaric acids.



Cleavage products are prevented by operating at lower temperature ranges. Thus 2,3-dihydropyran produces (242) the 2,3-diol. Epoxides have been isolated (363) in the oxidation of styrene with 99.2% hydrogen peroxide in t-butanol containing 1% osmium tetroxide catalyst. The products included phenyl glycol, styrene oxide, benzaldehyde, and benzoic acid. The oxide was obtained in 41% yield. Epoxy formation was said to be favored at low reaction temperatures with the use of high strength hydrogen peroxide.

Other examples of the use of metal-activated hydrogen peroxide include the oxidation of allyl compounds (66, 67, 83, 183, 184, 325, 391, 431), aliphatic hydrocarbons (344), cyclic dienes (334), sugar derivatives (229, 330), steroids (76, 143, 318), dibasic acids (333), and fatty oil derivatives (322). Special mention should be made of the possible hazard involved in the use (455) of acetone as a solvent. Cyclic peroxides of acetone are possible (502) byproducts of this reaction.

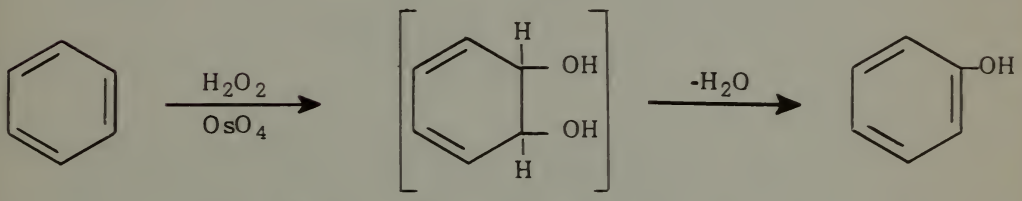
Typical Procedure for Hydroxylation (107)

Dissolve maleic acid or its anhydride in water to give a solution containing about 30% maleic acid. Add a dilute aqueous solution of potassium tungstate calculated to provide 0.5% WO_3 (based on maleic acid). Add a quantity of 35% commercial hydrogen peroxide to the mixture so that a 50% excess of maleic acid is present. Maintain a temperature of 70°C. throughout the reaction, a period of 10-11 hours. If nearly complete consumption of hydrogen

peroxide is indicated at this time, gradually increase the temperature to reflux the mixture for one hour. Although 10-12 hours is required for complete hydroxylation, the reaction is 90% complete in 3 hours. To obtain racemic tartaric acid, cool the reaction mixture to effect crystallization of the product.

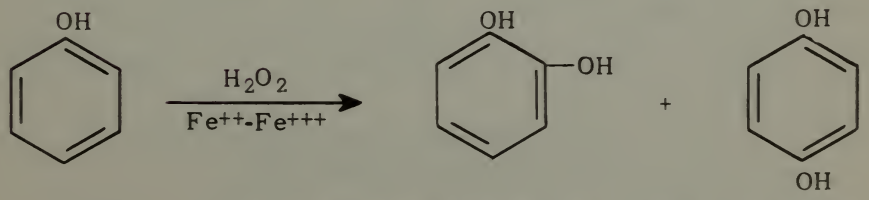
Hydroxylation of Aromatic Hydrocarbons

Aromatic rings are hydroxylated with both Fenton's and Milas' reagents although the mode of oxidation is probably different in each case. Fenton's oxidation of benzene may involve the intermediate formation of hydroxyl free radicals. The method of attack by Milas' reagent is uncertain but is said (324) to require formation of a dihydroxy intermediate which dehydrates to produce the monohydroxy compound.



The products formed, however, are easily predicted if metal-catalyzed hydrogen peroxide is considered to react by a primary dissociation into two hydroxyl radicals.

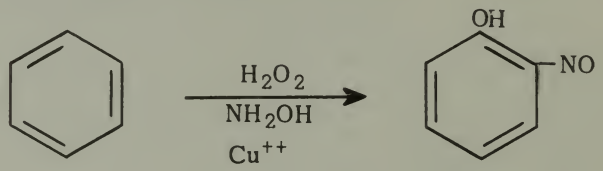
The oxidation of phenol (98) with hydrogen peroxide catalyzed by the Fe^{++}-Fe^{+++} couple produces (108, 364) catechol in yields as high as 30%. Other products found include the p-substituted derivative.



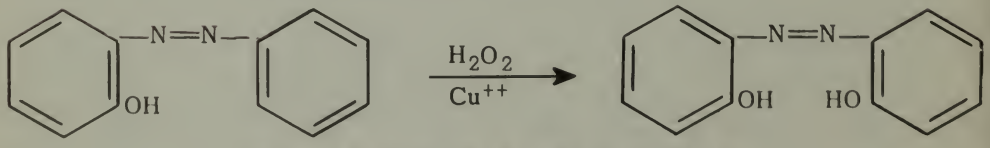
The distribution between the o- and p-substituted products is about equal although the p-product appears to predominate in acid systems. Formation of the m-derivative is generally excluded in acid (296, 316, 432). The tendency for oxidation of catechol to quinone is precluded by the use (364) of aluminum acetate to inactivate the catechol produced by the primary oxidation.

Aromatic hydrocarbons such as benzene and toluene are hydroxylated (114, 324) with hydrogen peroxide catalyzed by OsO_4 in t-butanol in about 30% yields. Polynuclear hydrocarbons like anthracene are converted quantitatively to anthraquinone, probably through oxidation of the hydroxylated intermediate by excess peroxide.

Copper compounds have also been used to catalyze the hydroxylation of benzene. In the presence of hydroxylamine, benzene is converted (284) to o-nitrosophenol by the action of hydrogen peroxide and hydroxylamine hydrochloride in the presence of copper sulfate.



Hydroxylation is presumably effected by hydroxyl free radicals which also oxidize hydroxylamine, forming an active intermediate to nitrosate the ring. Pernitrous acid, known (212) to be formed by the action of hydrogen peroxide on nitrogen oxides, is probably not involved in this reaction. Benzene and sodium benzoate treated with hydrogen peroxide and copper sulfate in like manner give (283) phenol and salicylic acid respectively. Dihydroxy azo dyestuffs are made (367) by treating the monohydroxy derivative with slightly acid hydrogen peroxide in the presence of copper salts.

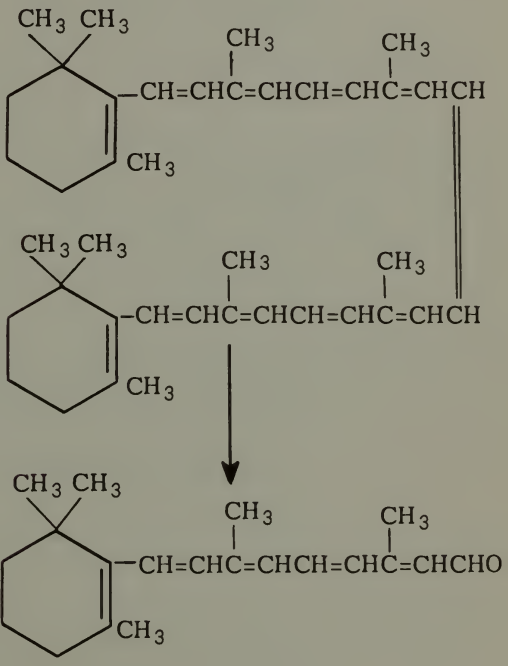


Typical Procedure for the Hydroxylation of Aromatic Hydrocarbons (367)

Dissolve 47.9 g. of o-hydroxy azobenzene in 500 g. of water. Run in a solution of 27.5 g. of copper sulfate in 300 g. of water, and add 30 g. of sodium acetate at 60°C. while stirring. Add 40% hydrogen peroxide solution (21.3 g.) in 100 g. of water over a period of 30 minutes. Salt out the copper complex and neutralize with strong hydrochloric acid solution. Crystallize the product.

Oxidative Cleavage – Unsaturated Bonds

Metal-catalyzed hydrogen peroxide effects the rupture of unsaturated bonds, presumably by cleaving an intermediate dihydroxy compound. Cleavage reactions usually require more vigorous conditions than are used in hydroxylation reactions. The unusual specificity of osmium tetroxide is shown (313, 480) in the cleavage of β-carotene with hydrogen peroxide to give vitamin A aldehyde in about 30% yields. Peracetic acid also converts (50) β-carotene to the aldehyde, but yields are low (0.5%).



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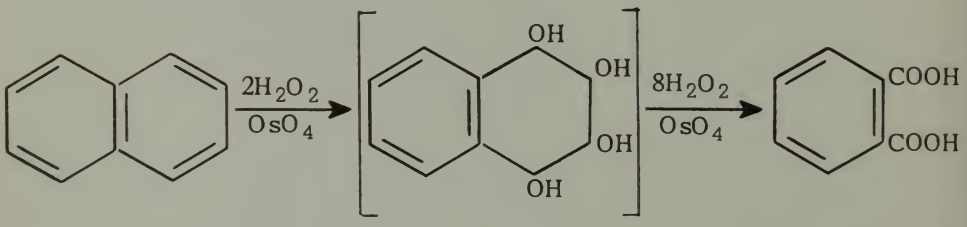
The aldehyde is important as a source of the biologically active vitamin A alcohol. The alcohol (vitamin A) is found in such materials as butter, egg yolk, and cod-liver oil and is necessary for the growth and survival of human beings. Vitamin A also prevents rickets and xerophthalmia. Vitamin A activity shown by such foods as yellow corn and butter is due to β-carotene, which is probably converted to vitamin A in the liver of animal organisms. Vitamin A was first synthesized in 1937 by a series of reactions beginning with β-ionone.

Other cleavages effected by hydrogen peroxide include the conversion of cyclohexene to adipic acid (324) in 35% yields and isoeugenol to vanillin (326) in 66% yields.

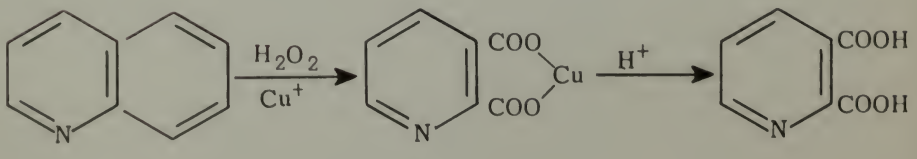
Oxidative Cleavage – Aromatic Rings

Aromatic rings are cleaved (324) oxidatively by metal-catalyzed hydrogen peroxide. The reaction depends upon the use of excess hydrogen peroxide, a metal oxide peracid-former as catalyst, and reaction temperatures from 80°-100°C. The tetrahydroxy derivatives are probably formed as intermediates.



Non-aqueous solvents, including t-amyl and t-butyl alcohols, acetonitrile, and the higher boiling ethers, are used in the reaction. Hydroquinone is converted to quinhydrone with hydrogen peroxide at low concentrations of tungstic, molybdic, and vanadic acid catalysts. At the higher concentration levels of tungstic acid, hydroquinone is converted (257) to maleic acid, however.

Quinolinic acid has been prepared (222) by the oxidative cleavage of quinoline.



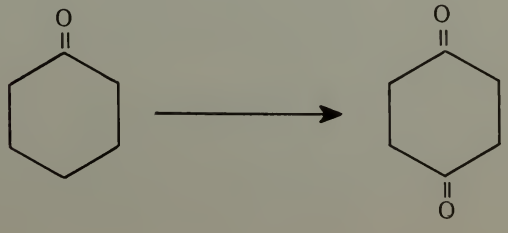
As expected, the great stability of the pyridine ring to oxidation is shown by the preferential cleavage of the benzene ring of quinoline. The reaction is carried out in acetic or formic acid solutions at 60°-70°C. Decarboxylation of quinolinic acid yields nicotinic acid (niacin), which – as the amide (niacinamide) – forms a part of the prosthetic group of enzymes (Coenzyme I and II) active in biological systems. From a pharmacological view, the amide is more easily supplied to the human organism because large doses of the acid tend to cause a rise in body temperature. The vitamin, nicotinic acid, and the amide are valuable for the cure of human pellagra and blacktongue in dogs.

Typical Procedure for the Cleavage of Aromatic Rings (222)

Dissolve 26 g. of copper acetate monohydrate in 500 g. of water, and add 12 g. of quinoline dissolved in 18 g. of glacial acetic acid. Warm the copper acetate-quinoline solution to 60°C., and add 27.6% aqueous hydrogen peroxide solution (137.5 g.), maintaining the reaction temperature below 70°C. during the addition of the peroxide. When the evolution of gas ceases, filter off the blue precipitate of copper quinolinate. A yield of 17 g. of copper quinolinate dihydrate is obtained after washing and drying the precipitate.

Quinone and Ketone Formation

As mentioned, metal-activated hydrogen peroxide gives quinones upon the oxidation of hydroxylated products (324). In a reaction not involving hydroxylation of an olefinic linkage, however, cyclohexanone has been converted to 1,4-cyclohexanedione by treatment with hydrogen peroxide in the presence of V_2O_5 at room temperature (456,465).



The maximum yield of the dione is about 35%. A large portion (40%) of the original cyclohexanone is recovered unreacted. Small amounts of adipic acid and its hemialdehyde are also isolated in the reaction.

Organic Sulfur Oxidation

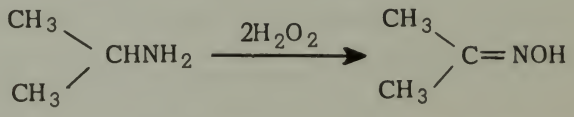
Valuable disulfide additives for lubricating oils have been prepared (410, 411) by oxidizing cuprous mercaptides with hydrogen peroxide.

$$2\text{RS-Cu} \xrightarrow[4\ \text{HCl}]{2\text{H}_2\text{O}_2} \text{R-SS-R}$$

High molecular weight, especially branched-chain, mercaptans are somewhat resistant to oxidation by hydrogen peroxide. The use of cuprous chloride alone to form the disulfide results in the formation of excessive amounts of cuprous mercaptide. Preformed cuprous mercaptides, however, are oxidized smoothly by hydrogen peroxide even though the mercaptans from which they are derived are of high molecular weight.

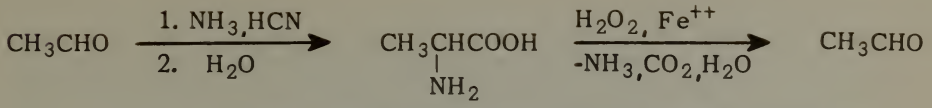
Organic Nitrogen Oxidation

Oximes are prepared (255, 369) by reacting a primary or secondary amine and hydrogen peroxide in the presence of salts of tungsten (WO_3), molybdenum (MoO_3), or uranium (UO_3) acids.



The reaction is exothermic, producing acetoxime as shown above in about 80% yields. Efficient control of the reaction temperature (0°-15°C.) is necessary to prevent decomposition of hydrogen peroxide and the formation of byproducts. The oxidation of amines to oximes has also been carried out (15) by use of Caro's acid. Oximes are ordinarily prepared by condensing aldehydes or ketones with hydroxylamine.

Hydrogen peroxide in the presence of ferrous sulfate degrades (409) α-amino acids at ordinary temperatures. The reaction – known as the Strecker degradation of α-amino acids – converts alanine to acetaldehyde, thereby reversing the Strecker cyanohydrin synthesis of alanine.



Similar results have been obtained using boiling persulfate solution or hydrogen peroxide in acid medium. Peracids and such organic peroxides as benzoyl peroxide effect degradation if the amino group is unsubstituted.

Typical Procedure for Nitrogen Oxidation (255)

Dissolve 59 g. of isopropylamine in 7.5% sodium tungstate solution (88.5 g.) and add 219.6 g. of an aqueous 29% hydrogen peroxide solution over a period of 2.5 hours. Maintain reaction temperature at 5°C. during the addition of peroxide and for a period of 30 minutes after the addition has been completed. Keeping the reaction mixture cooled with ice, neutralize the solution with sulfuric acid and extract with ether. Acetoxime (47 g.) is obtained from the ether extract.

Oxidation of Alcohols

Fenton's oxidation of organic compounds, employing hydrogen peroxide catalyzed by the Fe^{++}-Fe^{+++} couple, was originally established (164, 187) for the oxidation of alcohols to aldehydes.

A water-soluble alcohol like glycerine is thus converted to glyceraldehyde as shown above. A study (315) of the relative rates of reaction of alcoholic systems shows that the oxidation of isopropyl alcohol proceeds at a greater rate than n-propyl alcohol. Ethyl alcohol and n-propyl alcohol are oxidized at approximately the same rate though exceeding that of methanol. The relative rates of oxidation, however, are known to change with changing concentration ratios of hydrogen peroxide to alcohol. Fenton's oxidation of alcohols is carried out efficiently by adding ferrous salt solution dropwise to the alcohol-peroxide mixture containing sulfuric acid to maintain pH 1.0.

The use of hydrogen peroxide and OsO_4-type catalysts in t-butanol results (327) in the cleavage of vicinal dihydric alcohols. Propylene glycol, for example, forms acetaldehyde and formaldehyde under proper reaction conditions.

$$\begin{matrix} RCH\text{-}CH_2 \\ | \quad | \\ OH\ OH \end{matrix} \longrightarrow RCHO + CH_2O$$

Except for iron, however, the transition metal catalysts used for Milas' oxidations are not normally employed to oxidize alcohols with hydrogen peroxide.

Oxidative Dimerizations

Kharasch has shown (268) that the decomposition of diacetyl peroxide in monohydric alcohols causes a coupling of two solvent molecules producing dihydric alcohols. The diacetyl peroxide is believed to decompose forming methyl free radicals which abstract hydrogen from the carbon atom alpha to such activating groups as hydroxyl, carboxyl, nitrile, ester, and ketone functions. The substrate free radicals formed by hydrogen abstraction then undergo coupling. The alcohol molecules, however, are also oxidized to aldehydes and ketones by the $CH_3\bullet$ radical in the coupling reaction.

$$CH_3CO\text{-}OO\text{-}COCH_3 \longrightarrow 2CH_3COO\bullet \longrightarrow CO_2 + 2CH_3\bullet$$

$$CH_3\bullet + RCH_2OH \longrightarrow \underset{\bullet}{RCHOH} + CH_4$$

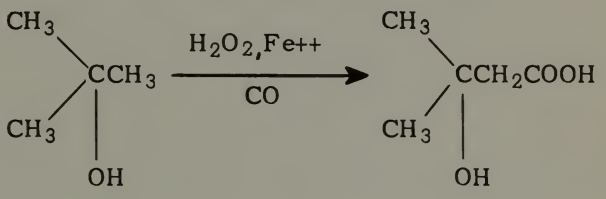
$$2\underset{\bullet}{RCHOH} \longrightarrow \begin{matrix} RCHOH \\ | \\ RCHOH \end{matrix}$$

The reaction is termed "α-coupling" and is effected by certain organic peroxides (68).

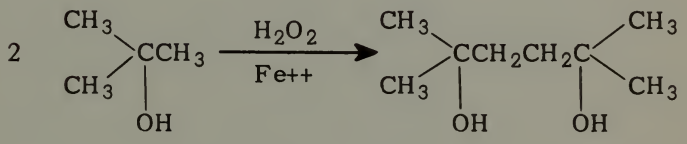
Jenner has found (248) that hydrogen peroxide, producing hydroxyl free radicals by the action of Fe^{++}, causes "β-coupling".

$$2RCH_2CH_2COOH \xrightarrow[Fe^{++}]{H_2O_2} \begin{matrix} RCHCH_2COOH \\ | \\ RCHCH_2COOH \end{matrix}$$

The reaction is useful for the preparation of such difunctional compounds as adipic acid to be used for polyamide manufacture. The principle of β-coupling is again shown (112) in the preparation of β-hydroxy isovaleric acid from t-butanol and carbon monoxide.



As might be expected, an equal quantity of tetramethyltetramethylene glycol is obtained.



Typical Procedure for Oxidative Dimerization (248)

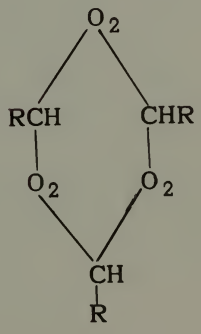
To a solution of 495 g. of propionic acid in 100 g. of water, add with stirring two separate solutions of (a) 41 g. of hydrogen peroxide in 96 g. of water (137 g. of 30% hydrogen peroxide) and (b) 334 g. of ferrous sulfate heptahydrate in 1000 g. of water containing 118 g. of concentrated sulfuric acid. Cause solutions (a) and (b) above to be added simultaneously and proportionately over a period of 30 minutes while maintaining a reaction temperature of 25°C. Now add 48 g. of sodium hydroxide in 44 g. of water and extract the resulting solution five times with methyl ethyl ketone. Distill off methyl ethyl ketone and propionic acid, and obtain adipic acid as crystals from the residue (40 g.) in the still pot. A small amount of 2,3-dimethylsuccinic acid is also obtained in the reaction.

PREPARATION OF ORGANIC PEROXIDES

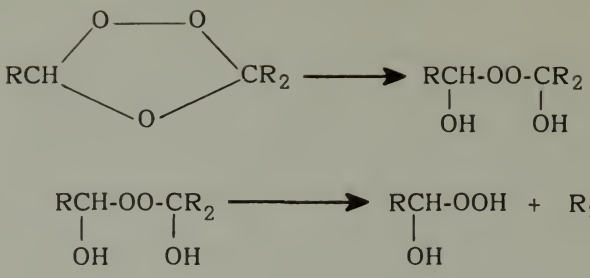
Organic peroxides may be defined as derivatives formed by replacing one or both hydrogen atoms of hydrogen peroxide by organic radicals. The physical properties (118) of organic peroxides are not well known. They exhibit boiling points tending to be higher than those of the oxygen compound to which they correspond. Many organic peroxides, however, explode before their atmospheric boiling points are reached. The low molecular weight hydroperoxides and peracids are water-soluble, but the hydroperoxy group appears to be less hydrophilic than the hydroxyl group. The dialkyl peroxides are less water-soluble than the hydroperoxides of comparable molecular weight. Many hydroperoxides, except t-hydroperoxides, nave acid character and form salts. Hydroperoxides are distinguished from dialkyl peroxides by their susceptibility to attack by lead tetraacetate. Hydroperoxides are also easily reduced to the corresponding alcohols. The organic peroxides tend to explode under many conditions, especially in the crystalline state. The explosibility of the peroxides appears to be related to the proportion of active oxygen carried by the peroxide molecule as well as to its physical state. Organic peroxides are prepared by methods including the addition and substitution reactions of hydrogen peroxide.

The organic peroxides which are prepared directly from hydrogen peroxide are illustrated in the following table. The organic substrates from which the various peroxides are obtained in reactions with hydrogen peroxide are also indicated.

Organic Substrates	Peroxy Products
Acids RCO-OH	Peracids RCO-OOH
Alcohols R-OH	Hydroperoxides R-OOH
Alcohols R-OH	Dialkyl peroxides R-OO-R
Acid anhydrides, Chlorides RCO-O-COR, RCOC1	Diacyl peroxides RCO-OO-COR

Aldehydes, Ketones RCHO, RR'CO	Hydroxyalkyl hydroperoxides RR'C(OH)-OOH
Aldehydes, Ketones RCHO, RR'CO	Hydroxy hydroperoxyalkyl peroxides RCH(OH)-OO-CHR(OOH)
Aldehydes, Ketones RCHO, RR'CO	Bis(hydroxyalkyl)peroxides RCH(OH)-OO-CHR(OH)
Aldehydes, Ketones RCHO, RR'CO	Alkylidene peroxides 
Alkyl chloroformates C1-CO-OR	Dialkyl peroxycarbonates ROCO-OO-COOR

Alkyl polyperoxides and transannular peroxides obtained by auto-oxidation, and such peroxides as peroxy acetals requiring the isolation and further reaction of hydroperoxides, are not included in the above table. Certain of the peroxides listed above have also been obtained in reactions not involving hydrogen peroxide. Thus Rieche prepared bis(hydroxylalkyl) peroxides and hydroxyalkyl hydroperoxides by the hydrolytic cleavage of isozonides.



The hydroxyalkyl hydroperoxide is formed in the secondary cleavage reaction as shown above.

There are four general methods of incorporating the peroxide bond (-OO-) into organic molecules. These methods include auto-oxidation (487), ozonization, (118), the association of oxygenated free radicals (265), and the addition and substitution reactions of hydrogen peroxide and hydroperoxides (118). The reactions of hydrogen peroxide leading to the formation of organic peroxides are outlined in the following paragraphs and include those with acids, anhydrides, esters, alcohols, organic sulfates and sulfonates, carbonyl compounds, and organic chlorine compounds.

Reaction with Organic Acids, Anhydrides, and Esters

The reactions of acids, anhydrides, and esters with hydrogen peroxide ordinarily lead to the formation of organic peracids although other organic percompounds may result. Peracids are usually prepared, however, by mixing hydrogen peroxide and aliphatic acids in the presence of strong acid catalysts. A complete description of the preparation of peracids has been given by Swern (437).

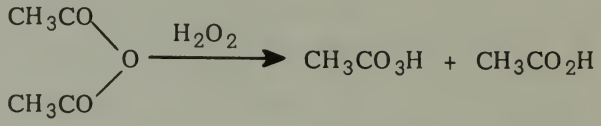
Mixing hydrogen peroxide and an organic acid such as glacial acetic acid results in an equilibrium formation of peracetic acid, hydrogen peroxide, water, and acetic acid as follows:

The conversion of hydrogen peroxide to peracetic acid at a constant temperature depends upon the ratio of glacial acetic acid to hydrogen peroxide. In the absence of a strong acid catalyst, the attainment of equilibrium varies markedly with the organic acid employed. Mixtures of hydrogen peroxide and glacial acetic acid may require seven days for attainment of equilibrium without the benefit of a catalyst. Maximum conversions to performic acid, on the other hand, are obtained in one to three hours in the absence of catalysts using a large excess of formic acid. Uncatalyzed mixtures of hydrogen peroxide and propionic acid may not reach equilibrium within fourteen days at ordinary temperatures. The rate of equilibrium formation of peracid, therefore, decreases with decreasing acid strength of organic acid.

Equimolar mixtures of high strength hydrogen peroxide and acetic acid with 1% sulfuric acid catalyst reach equilibrium after standing for twelve to sixteen hours. A more convenient method for the preparation of peracetic acid consists of passing hydrogen peroxide and acetic acid through a cation exchange resin bed. The method, which can be operated continuously or batchwise, has been developed (150) in the Du Pont laboratories to complement the hydrogen peroxide-resin procedure for epoxidation. It is a suitable method for the preparation of dilute peracid solutions but requires high strength hydrogen peroxide for more concentrated peracid solutions.

The resin technique for peracetic acid formation is operated simply by passing a mixture of glacial acetic acid and hydrogen peroxide through a cation exchange resin column. The column contains polystyrene sulfonic acid resin (acid form, medium porosity) which has been treated with glacial acetic acid to remove excess water. The effluent peracetic acid solution is adjusted to give the hydrogen peroxide-acetic mixture the proper contact time with the resin bed. Contact time is defined as the volume of the resin bed divided by the rate of product take-off. Under conditions for operation of the resin technique, a contact time of twelve to sixteen minutes (at 45°C.) is sufficient for maximum conversion of hydrogen peroxide to peracetic acid.

Peracetic acid has been prepared (209) by mixing 90% hydrogen peroxide and acetic acid in the presence of sulfuric acid and adding acetic anhydride to displace equilibrium by removing water. The use of acetic anhydride adds to the hazards of the reaction by increasing the exotherm. The possibility of forming byproduct diacetyl peroxide by use of excess acetic anhydride also exists. Peracetic acid is also prepared (128) in a shorter time by the complete substitution of acetic anhydride for glacial acetic acid in the peracid reaction.

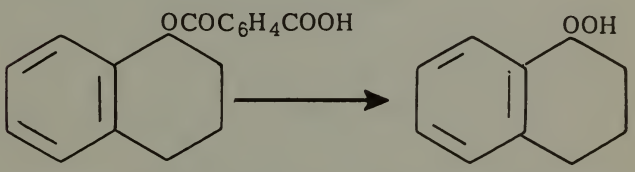


Diacetyl peroxide is formed in the reaction and may be hydrolyzed by use of sulfuric acid catalyst and temperatures (35^{o}-40^{o}C.) above the ordinary. In the experience of the author, however, the use of acetic anhydride under these conditions results in peracid solutions containing diacetyl peroxide, which have exploded.

The higher molecular weight peracids are sometimes difficult to prepare. Swern and co-workers have prepared (359) C_6 tc C_{18} peracids such as perlauric acid (61% to 99% yields) by mixing fatty acids with hydrogen peroxide in concentrated sulfuric acid. These and other peracids apparently exist (445) as 5-membered intramolecularly chelated rings as shown by infrared, X-ray diffraction, and molecular weight studies. Trifluoroperacetic acid has been prepared (155, 156, 157, 159) by mixing hydrogen peroxide and trifluoroacetic acid or trifluoroacetic anhydride. Trifluoroperacetic acid has shown excellent oxidizing properties in preparing such compounds as epoxides and N-oxides. Perbenzoic acid is best prepared (127) by the cleavage of dibenzoyl peroxide with sodium alcoholates or by treating (195) benzoyl chloride with aqueous sodium peroxide. The explosive dibenzoyl peroxide, however, is involved in both reactions; in the first, as a raw material and in the second, as a byproduct. Monoperphthalic acid has been obtained by dissolving (378) phthalic anhydride in aqueous hydrogen peroxide solutions (27.5%-35%) at 60^{o}-65^{o}C. The peracid is isolated by crystallization from the reaction mixture. Peracids in the camphoric acid series have been prepared (330) by reacting camphoric anhydride

in ether with sodium peroxide at 0°C. Dicamphoryl peroxide – which explodes when heated, giving terpene-like odors – is also formed in the reaction. Camphoric acid peracid adds quantitatively to the double bonds of pinene and cholestorol, forming (331) epoxides.

Esters and hydrogen peroxide react to form peracids as well as hydroperoxides. Peracetic acid is produced (115) in the reaction of alkyl acetates and alkaline hydrogen peroxide (pH 11 or greater). The peracid is also obtained (379) by the reaction of alkaline hydrogen peroxide (pH 8-11) and the corresponding anhydride. Dissolving 1,2,3,4-tetrahydro-1-naphthyl hydrogen phthalate in 90% hydrogen peroxide containing sodium bicarbonate produces (131) the same hydroperoxide formed in the auto-oxidation of 1,2,3,4-tetrahydronaphthalene.

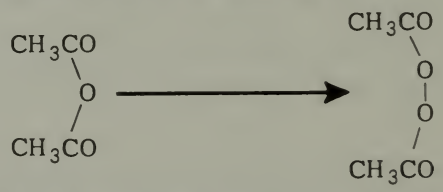


The reaction is believed to involve the nucleophilic attack of hydrogen peroxide on the ring C-atom.

A knowledge of the physical properties (437) of organic peracids is essential in contemplating the use of hydrogen peroxide in the reactions of the peracid systems. Of the organic peracid systems, peracetic, performic, and perbenzoic acids are the most used in organic syntheses. *Peracetic acid* is soluble in water and organic solvents. It has an intensely sharp odor and is irritating to the skin. Pure peracetic acid explodes when heated at 110°C.; peracetic acid in concentrations greater than 69% has shown propagating detonations when heated. Peracetic acid is considerably more stable to decomposition than performic acid. *Performic acid* is also soluble in water and in organic solvents. Its vapor is irritating to the mucous membrane and produces painful blisters in contact with the skin. Performic acid is more volatile than formic acid and explodes even in the absence of catalysts when heated rapidly to about 85°C. Solutions of performic acid of greater than 45% concentration have exploded upon the addition of small quantities of such catalysts as zinc dust and lead dioxide. Performic acid

solutions are unstable, losing its active oxygen rapidly even at 0°C. *Perbenzoic acid* is soluble in organic solvents and only slightly soluble in water. It has a strong odor similar to that of hypochlorous acid. Unlike the clear-liquid performic and peracetic acids, perbenzoic acid is a white solid obtained by crystallization from chloroform-ethanol or petroleum ether mixtures. It melts at 41°C. and may be distilled under vacuum with little decomposition. Perbenzoic acid is stable at room temperature but decomposes smoothly when heated at 80°-100°C. It does not explode on impact but has been exploded when heated in a steel bomb.

Dialkyl peroxides are prepared in high yields by the action of hydrogen peroxide on carboxylic anhydrides. Diacetyl peroxide has been prepared (393, 416) by adding sodium peroxide or hydrogen peroxide to acetic anhydride dissolved in a viscous ester such as dimethyl phthalate held at -5°C.

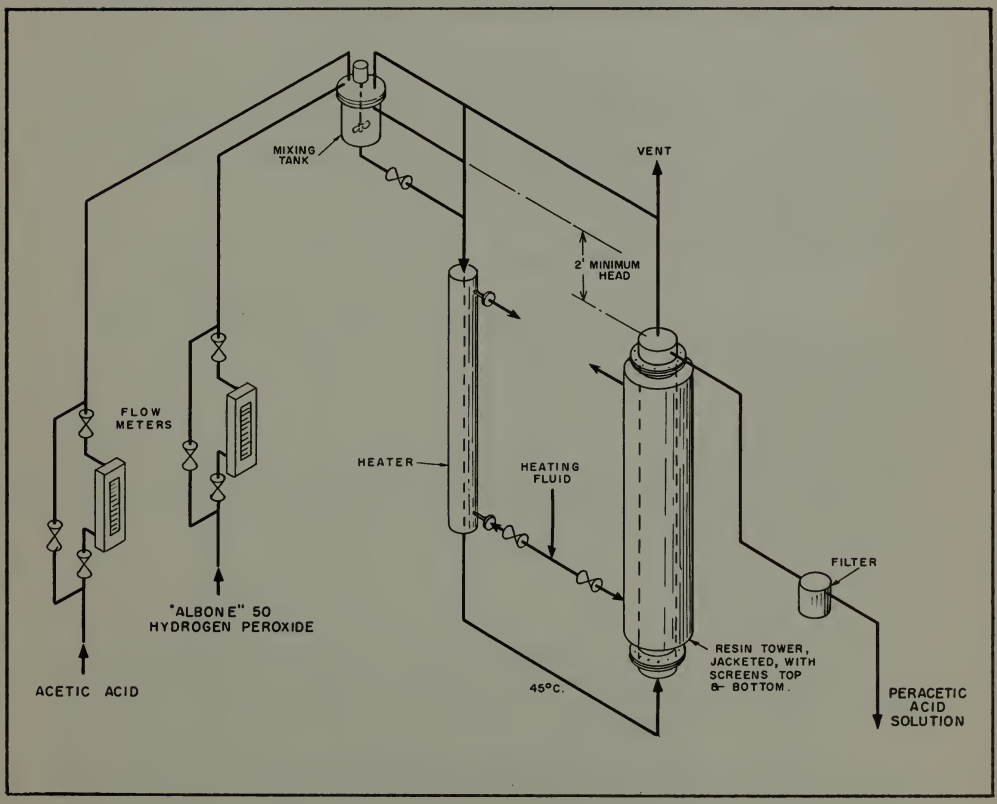


The use of the phthalate ester allows the formation of diacetyl peroxide in a nonflammable solvent which also prevents entrainment of the dangerous peroxide. The best yields of peroxide are obtained when sodium carbonate is used to maintain pH in the range of 4-7.5. Diacetyl peroxide is unstable and extremely sensitive to shock, decomposing with great shattering power (brisance). Crotonyl peroxide is formed (460) by mixing crotonic anhydride and 30% hydrogen peroxide under sufficient stirring to form an emulsion. The organic peroxide crystals separate (94% yield) upon the slow addition of 20% aqueous caustic solution at 0°C.

Typical Hydrogen Peroxide-Resin Procedure for the Preparation of Peracid (150)

With stopcock closed, add glacial acetic acid to a depth of about 3 inches in a column (1" x 12"). Charge acetic-treated polystyrene sulfonic acid resin (20-50 mesh) of medium porosity to a depth of six inches. By opening the stopcock drop the acetic acid level over the resin bed to a point even with the top of the bed. Circulate warm water through the jacket around the column to heat the resin bed to 45°C.

Add a mixture of glacial acetic acid and "Albone" hydrogen peroxide to the column from a suitable reservoir. Adjust product take-off by operating the stopcock at the bottom of the column to give a contact time of about 16 minutes. Contact time is defined as the volume of resin bed divided by the rate of product take-off. After a volume of peracetic acid solution equivalent to two resin volumes has been taken off, the effluent solution attains the equilibrium formation of peracetic acid.



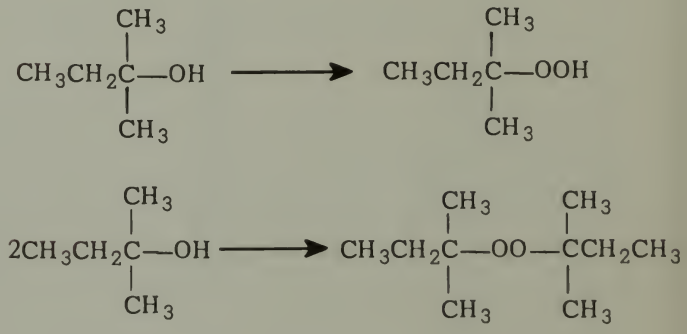
FLOW DIAGRAM: CONTINUOUS PREPARATION OF PERACETIC ACID

BY THE HYDROGEN PEROXIDE – RESIN TECHNIQUE

Reaction with Alcohols

A common procedure for the preparation of hydroperoxides and disubstituted peroxides consists of reacting (338) hydrogen peroxide and tertiary alcohols in strong sulfuric acid although catalytic quantities of acid have also been used (120). The reaction probably involves the formation of an intermediate sulfate and is, therefore, similar to the alkylation of hydrogen peroxide by dialkyl sulfates. The reactions often result in serious explosions, although the final products of such reactions are relatively stable. The peroxide products are not readily formed from primary or secondary alcohols.

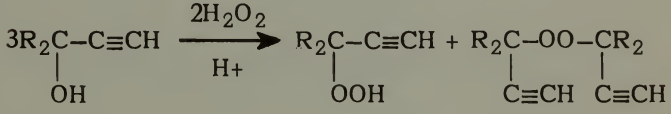
The reaction can be carried out by adding aqueous hydrogen peroxide to a mixture of tertiary alcohol and 70% sulfuric acid at 0°-5°C. Such peroxides as t-amyl hydroperoxide and di-t-amyl peroxide are prepared (338) in this manner.



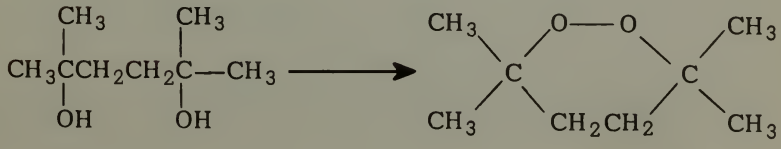
t-Amyl hydroperoxide is used as a starting material in reacting with benzoyl chloride and potassium hydroxide to prepare t-amyl perbenzoate. Other peroxides prepared by reacting hydrogen peroxide and alcohols in sulfuric acid include triethylmethyl and pentamethylethyl hydroperoxide (336), 1-methylcyclohexyl hydroperoxide (336), and t-butyl hydroperoxide (337). Certain tertiary alcohols treated with hydrogen peroxide have given (265) phenols and ketones as products of the reaction, probably indicating that an intermediate peroxide has been decomposed under acid catalysis. Mixtures of tertiary alcohols and hydrogen peroxide have been used (320) as germicides, fungicides, bleaching agents, and peroxide reagents.

Strong sulfuric acid used in the hydrogen peroxide-alcohol reaction may be replaced (411) by heteropolyacids having multiple inorganic acid radicals. The heteropolyacids, which are soluble in ether, contain the elements of phosphorus, silicon, or boron coordinated with a metallic oxide such as tungsten oxide. The characteristic solubility of heteropolyacids allows the preparation of alkyl hydroperoxides to be carried out in ether. The use of heteropolyacids minimizes the formation of undesirable byproducts and permits the use of higher reaction temperatures (32). The use of such organic solvents as ether and chloroform (315) improves the efficiency of the reaction of hydrogen peroxide and alcohols.

Carbinols of many types have been converted (130) to hydroperoxides and disubstituted peroxides. Acetylene peroxides are formed in the interaction of hydrogen peroxide and the hydroxyl group of acetylenic carbinols. These peroxides produced under acid catalysis are unusually stable despite the presence of the acetylenic bond (82, 328, 329).



Cyclic peroxides are produced (121) by the action of 50% hydrogen peroxide and strong sulfuric acid on such diols as 1,1,4,4-tetramethyl tetramethylene-1,4-diol.



The cyclic peroxides are remarkably stable and can be distilled in small quantities at atmospheric pressure without decomposition.

Typical Procedure for the Reaction of Alcohols (31)

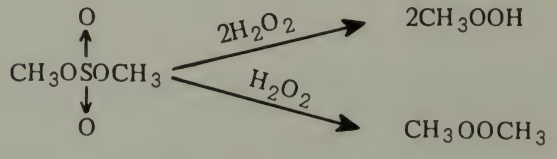
Mix t-butyl alcohol and 50% hydrogen peroxide in an equimolar ratio. Add 1.3 volumes of chloroform to each volume of the peroxide-alcohol mixture, and follow with the addition of 70% sulfuric acid in the

molar ratio of 0.5:1 of acid to t-butanol. Maintain the mixture at a reaction temperature of 60°C. for 20 minutes, and then cool rapidly. Separate the aqueous and the organic phases, and evaporate the chloroform to obtain the hydroperoxide product in 97% purity (86% conversion).

Reaction with Organic Sulfates and Sulfonates

Dialkyl sulfates and alkyl hydrogen sulfates produce hydroperoxides and dialkyl peroxides in reaction with alkaline hydrogen peroxide. This method is especially suitable for the preparation of the lower peroxides. Primary and secondary peroxides are better prepared by alkylation of hydrogen peroxide with alkyl sulfonates. Peroxides of this type are useful as polymerization catalysts and diesel fuel additives. They also play an important part in the study of combustion, gasoline burning, and air oxidation.

Baeyer and Villiger first attempted (14) the preparation of methyl hydroperoxide by treating hydrogen peroxide in alkaline solution with dimethyl sulfate. Upon evaporation of the reaction mixture with barium hydroxide added, a salt-like residue was obtained which detonated violently. Rieche and Hitz (384) isolated methyl hydroperoxide safely by treating 10% hydrogen peroxide in dimethyl sulfate with potassium hydroxide and distilling the acidified solution. This procedure avoids the preparation of the unstable barium salt.

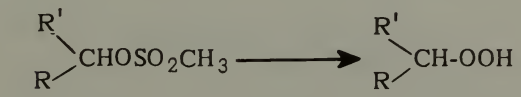


Methyl hydroperoxide has an extremely penetrating odor, attacking the respiratory organs to produce burns which heal with difficulty. In the vapor form, it attacks organic compounds and such metals as mercury. Methyl hydroperoxide explodes violently on heating and is very sensitive to shock, especially at higher temperatures. Surfaces with sharp angles have been known to cause the peroxide to explode. Methyl hydroperoxide reacts with formaldehyde to produce hydroxydimethyl peroxide which also explodes (384) violently on heating.

$$CH_2O + CH_3OOH \longrightarrow HOCH_2OOCH_3$$

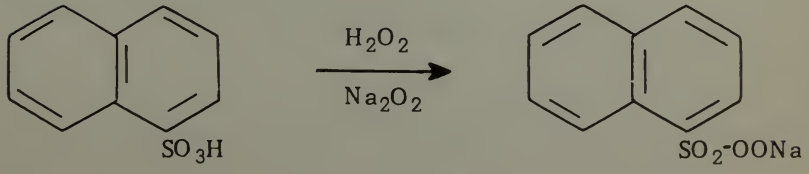
Such dialkyl peroxides as dimethyl, ethyl methyl, diethyl, dipropyl, and diisopropyl peroxides have been prepared (312, 321, 492, 493) in a similar fashion. Because of the explosive nature of these peroxides, manufacturing operations are carried out under an inert atmosphere and behind suitable barricades.

Primary and secondary dialkyl peroxides are effectively prepared (479) by the alkylation of hydrogen peroxide with alkyl methane sulfonates in aqueous alkaline methanolic solution. The method is one of the few producing (101) acceptable yields of pure hydroperoxides. Dialkyl peroxides prepared by this technique are more stable to mineral acids but apparently labile to alkali.



Yields of 38%-45% for n-alkyl hydroperoxides, 9%-52% for secondary hydroperoxides, and 45%-65% for dialkyl peroxides have been reported (496). A small sample of n-octyl hydroperoxide prepared by the alkyl sulfonate technique detonated (496) mildly during distillation at 68°C. (2 mm.).

Sodium peroxy sulfonates have been prepared (243) by reacting such sulfonic acids as naphthalene sulfonic acid and sodium peroxide in aqueous medium.



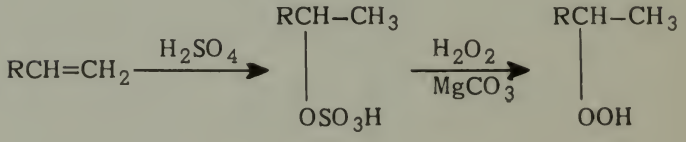
The operation is conducted in the cold to reduce the violence of the reaction. The peroxy product obtained has approximately 6% active oxygen and has been suggested as a possible bleaching agent or insecticide.

Typical Procedure for Preparation of Peroxides from Sulfonates (269)

Add 10 g. of 50% aqueous potassium hydroxide with cooling to a mixture of 40 g. of 30% hydrogen peroxide, 0.08 mole of alkyl methane sulfonate, and aqueous methanol. Maintain the mixture at room temperature for 20 hours. Keeping the mixture cool, add 30 g. more of 50% aqueous potassium hydroxide, and extract the reaction mixture with 50 ml. of benzene or hexane (for n-octyl hydroperoxide). Neutralize and dry the extract; then distill behind protective screens. Note: distillation of all peroxides should be considered hazardous.

Reaction with Olefins

Olefins have been transformed to hydroperoxides in a reaction which amounts to the addition of hydrogen peroxide to the double bond. The reaction, however, is conducted in strong sulfuric acid and probably involves the formation of an intermediate sulfate.



The method is useful (321) because it eliminates the need for prior formation of neutral dialkyl sulfates which are often difficult to obtain.

Isooctyl hydroperoxide is prepared (233) by mixing diisobutylene with aqueous sulfuric acid and hydrogen peroxide.

If the acid concentration of the aqueous phase is maintained above 45%, the isooctyl hydroperoxide rearranges to form neopentyl alcohol and acetone. The hydroperoxide has been isolated, however, at below 45% strengths of acid. A violent explosion has been reported (348) in the above reaction, presumably caused by the formation of acetone peroxide.

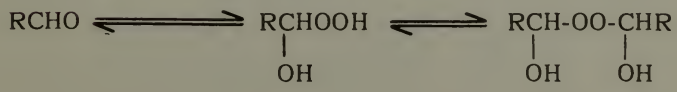
Typical Procedure for the Preparation of Olefin Hydroperoxides (321)

Add one mole of isobutylene over a period of 30 minutes to two moles of 70% sulfuric acid at -10°C. Provide adequate agitation during the addition of isobutylene. Add slowly two moles of hydrogen peroxide and allow to stand at 0° to -5°C. for several hours. Neutralize the mixture with magnesium carbonate and isolate t-butyl hydroperoxide (44.3% yield) from the nonaqueous layer.

Reaction with Carbonyl Compounds

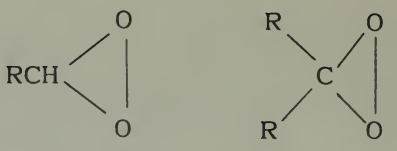
Hydrogen peroxide and aliphatic aldehydes ordinarily react to form carboxylic acids. The reaction proceeds through the intermediate formation of the hydroxy hydroperoxide which undergoes dehydration. Whether or not the primary peroxide is formed as a stable product often depends upon the choice of reaction solvent. Nonaqueous solvents increase the stability of the intermediate peroxide although acetaldehyde and chloral almost always form (11, 12) polymeric peroxides regardless of the reaction medium.

The following equilibrium is shown in mixtures of aldehydes (or ketones) and hydrogen peroxide.



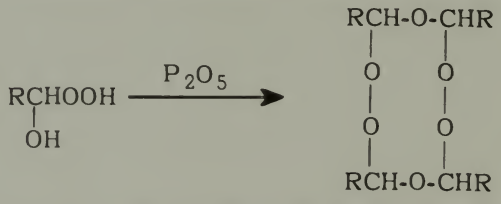
aldehyde *hydroxyhydroperoxide* *bis(hydroxyalkyl)peroxide*

The formation of the hydroxy hydroperoxide is favored in ether and may be isolated (382) under the proper conditions. Monomeric aldehyde or ketone peroxides, (A) and (B) page 90, are unknown and are probably incapable of existing.

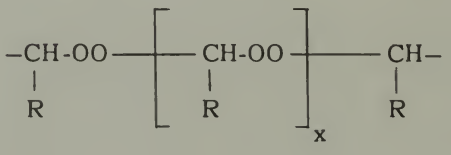


(A) (B)

If such peroxides are formed transiently, they dimerize or change into polymeric cyclic peroxides. Hydroxyalkyl hydroperoxides yield alkylidene peroxides when treated (72) with dehydrating agents.



The cyclic alkylidene peroxides are capable of further transformation to linear polymeric peroxides.

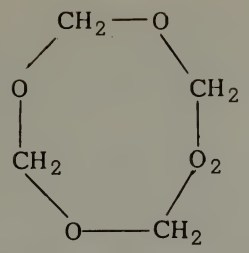


Heating hydroxyalkyl hydroperoxides, obtained by mixing equimolar amounts of an aliphatic aldehyde and hydrogen peroxide in ether, gives (429) carboxylic acids in yields usually exceeding 50%.

Formaldehyde treated (386) with hydrogen peroxide in ether in the presence of P_2O_5 forms bis (hydroxymethyl) peroxide bis(hydroxymethyl)ether.

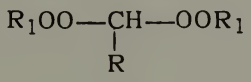
$$CH_2O \xrightarrow[P_2O_5]{H_2O_2} HOCH_2OCH_2\text{-}OO\text{-}CH_2OCH_2OH$$

This material has the consistency of liquid paraffin, is easily soluble in water, and does not appear to be particularly explosive. Upon continued treatment with P_2O_5 in ether, the bis-peroxide is probably converted to pertrioxymethylene, which is water-insoluble and very explosive.



pertrioxymethylene

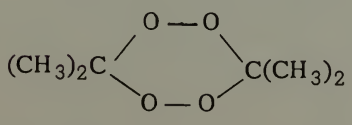
Bis(hydroxyethyl)peroxide treated (385) with P_2O_5 in ether gives a peroxyacetal having the composition of a dimeric butylene ozonide.

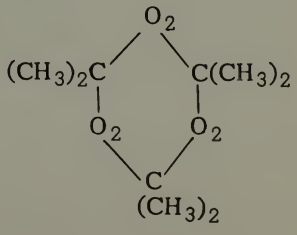


peroxyacetal

Upon standing for a long period in an open vessel, the peroxyacetal assumes the consistency of glycerine and becomes much more explosive.

The properties and methods of preparation of ketone peroxides are similar to those of the aldehyde peroxides. Trimeric acetone peroxide is prepared by mixing acetone and equivalent amounts of hydrogen peroxide and nitric acid. Cooled inadequately or carried out with excess nitric acid, the reaction proceeds explosively. Dimeric peroxide is also formed in the reaction.

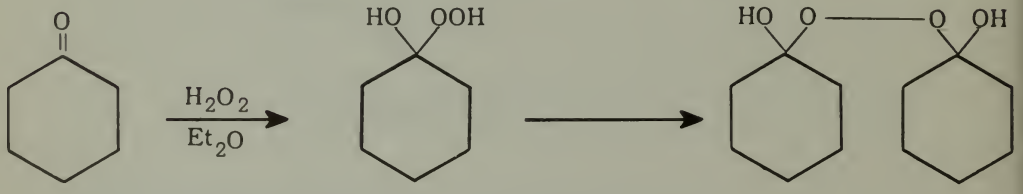


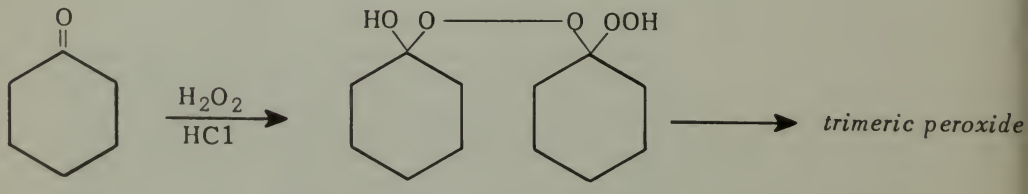


dimeric acetone peroxide *trimeric acetone peroxide*

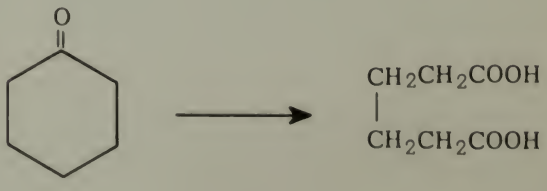
Both peroxides explode violently on impact, on treatment with concentrated sulfuric acid, or on being heated suddenly. Peroxides which have been prepared by the reactions of hydrogen peroxide and ketones include methyl ethyl ketone (44, 140), chloracetone (11,12), acetone (10 , 11, 12, 44, 140, 290, 401, 402), methyl propyl ketone (360), diethyl ketone (11, 12, 44), dipropyl ketone (11, 12, 140), diisobutyl ketone (140), methyl (β-phenylethyl) ketone (140), and dibenzyl ketone (140) peroxides.

Cyclic ketones behave as aliphatic ketones in their tendency to form stable but hazardous peroxides. The peroxides of cyclic ketones are obtained (332) best by the use of dry ethereal solutions of hydrogen peroxide as in the case of cyclohexanone.





The primary peroxides of cyclic ketones often rearrange in acid or alkali although this does not always occur. Hydrogen peroxide in aqueous solution, especially with persulfuric acid as catalyst, oxidizes cyclic ketones to dicarboxylic acids.

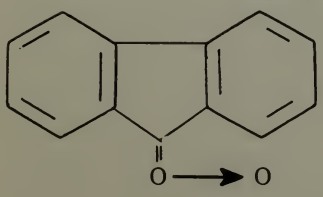


cyclohexanone *adipic acid*

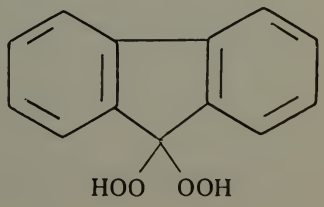
Commercial cyclohexanone peroxide, prepared by the auto-oxidation of cyclohexanol, is said (72) to be a complex mixture of hydroperoxides and disubstituted peroxides.

Cyclic peroxides which have been prepared include those of cyclopentanone (44), cyclohexanone (44, 140, 433), 2-methyl cyclohexanone (140), 3-methyl cyclohexanone (11, 12, 44), 4-methyl cyclohexanone (140), cycloheptanone (11,12), and exaltone (396, 433). The methyl cyclohexanones yield highly explosive peroxide oils upon treatment with hydrogen peroxide. The higher cyclanones do not react readily with hydrogen peroxide. Exaltone (cyclopentadecanone), heated with hydrogen peroxide in acid medium, gives (433) products similar to those formed in the reaction of hydrogen peroxide and cyclohexanone. Uses for the peroxide derivatives of cycloalkanes which have been suggested (446) include explosives, reaction accelerators, germicides, and bleaching agents.

Aromatic aldehydes in reacting with hydrogen peroxide often produce such final products as phenols or benzoic acid derivatives. The use of Caro's acid (H_2SO_5) in oxidizing aromatic aldehydes, however, usually results (140) in the formation of dimeric peroxides. Aromatic ketones or aldehydes, as a rule, are less likely to form stable peroxides than aliphatic carbonyl compounds because of the greater ease of migration of phenyl radicals attached to the carbonyl carbon. In the aliphatic series, the primary hydroxy hydroperoxide tends to be stabilized by dimerization or polymerization. Peroxides of such aromatic carbonyl compounds as acetophenone (140) and fluorenone (501) have been prepared, however. The peroxide of fluorenone has been described (500) as having an oxo-oxide structure (B) analogous to the amine oxides. If so, this structure would represent the first example of a derivative of the tautomeric formula $H_2O \longrightarrow O$.



(B)



(C)

Based on various tests, the structure of fluorenone peroxide is believed (122) to be that of a bis-hydroperoxide (C) (see page 93).

Certain ketone peroxides have been prepared by use of thio derivatives. Thus benzophenone peroxide results (256) upon adding thiobenzophenone at 15°C. to a mixture of concentrated sulfuric acid and aqueous hydrogen peroxide (35%). Thiourea treated with hydrogen peroxide in acetic acid yields (44) a product which decomposes explosively on drying.

Reaction with Organic Chlorine Compounds

Organic chlorine compounds reacting with hydrogen peroxide produce organic peroxides. The reaction is generally conducted in the presence of a chlorine acceptor which may be caustic or organic bases such as pyridine. The principal use of the reaction is to prepare diacyl peroxides from acyl halides. The reaction can be used (195), however, to prepare the monosubstituted acyl peroxide (peracid) although a considerable quantity of the diacyl product forms as a byproduct. Tertiary halides are also reactive, producing monosubstituted and disubstituted peroxides.

Acyl halides react with aqueous sodium peroxide or alkaline hydrogen peroxide, forming the corresponding diacyl peroxide. The reaction must be conducted in the cold to reduce its vigor.

$$2RCOCl \xrightarrow[2NaOH]{H_2O_2} RCO\text{-}OO\text{-}COR + 2NaCl + 2H_2O$$

The preparation of diacyl peroxides has been improved (181) by the use of suitable dispersing agents for the acid chloride. Such dispersants include oleic acid, ricinoleic acids, and lecithin. The use (196) of buffered systems to maintain pH between 6 and 9 is also a useful technique in preparing diacyl peroxides. Reacting (70) equimolar quantitites of benzoyl chloride and sodium peroxide in the attempt to prepare the peracid usually produces about three moles of perbenzoic acid for each mole of byproduct benzoyl peroxide. Difuroyl peroxide has been prepared (335) in 96% yield by mixing furoyl chloride and sodium peroxide in aqueous solution at 3°C. The peroxide, which is purified by shaking with sodium

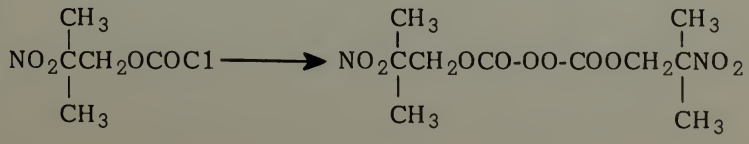
carbonate in ether solution, explodes violently upon being heated or rubbed. Like dibenzoyl peroxide (127), difuroyl peroxide is converted (335) to the peracid in high yield by treatment at -5°C. with sodium alcoholate. A peroxide mixture having the consistency of butter has been prepared (280) by reacting hydrogen peroxide and the acid chlorides of the total acids of cocoa butter. This peroxide mixture has a stability approaching that of benzoyl peroxide. However, it exhibits little of the oxidizing power characteristic of peroxides and is in fact useful in inhibiting oxidation. Use of cocoa butter peroxides to inhibit rancidity, to prevent gum formation in petroleum oils, and to deter aging phenomena has been suggested (280). These peroxides also show greater germicidal properties than such peroxides as benzoyl peroxide, which has little germicidal activity. Other diacyl peroxides which have been prepared include phthalyl peroxide (395), adipoyl peroxide (358), and substituted benzoyl peroxides (64, 225, 310, 489, 490).

A new method (138, 300, 469) for the preparation of diacyl peroxides involves the reaction of the dicyclohexylamine-hydrogen peroxide or the urea-hydrogen peroxide complexes and an acyl halide. The complexes are ether-soluble which allows the reaction to be conducted under anhydrous conditions.

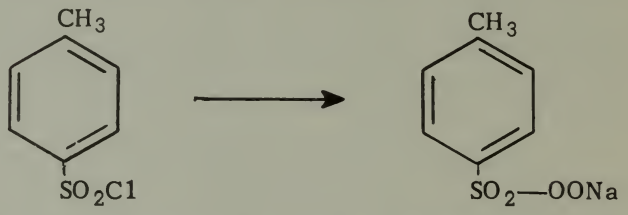
$$C_6H_5COCl \xrightarrow{NH_2CONH_2 \bullet H_2O_2} C_6H_5CO\text{-}OO\text{-}COC_6H_5$$

Use of the procedure has allowed the conversion of the acid chloride of trans-stilbene-2-carboxylic acid to the diacyl peroxide in 50%-55% yields. The usual procedures have not been successful in preparing this peroxide.

Organic chlorine compounds related to the acyl chlorides also produce organic peroxides. Peroxy dicarbonate derivatives have been prepared (43) by reacting an appropriate chloroformate derivative with hydrogen peroxide in the presence of alkali.



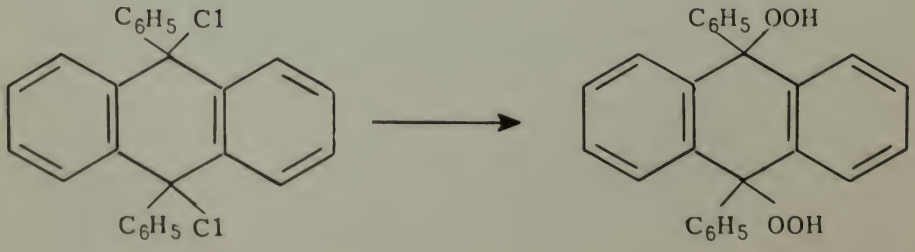
2-Nitro-2-methylpropyl chloroformate, prepared by reacting phosgene and the nitro-alcohol in dioxane, forms the corresponding peroxydicarbonate shown above. p-Toluene-sulfonyl chloride is converted (243) by sodium peroxide at low temperatures to the corresponding sodium persulfonate in 85% yields.



A related reaction is that of stearic acid sulfochloride and sodium peroxide, producing stearic acid persulfonic acid. The persulfonates are mentioned as possible bleaching agents and insecticides.

Dialkyl peroxides are prepared (247) by reacting alkaline solutions of hydrogen peroxide and alkyl halides dissolved in such solvents as methanol. Triphenylmethyl hydroperoxide has been obtained (488) in good yield by treating triphenylchloromethane with a slight excess of hydrogen peroxide.

The pure hydroperoxide is very stable, but slight impurities cause its decomposition to form phenol and phenyl ketone. The same products are formed by heating the peroxide to a temperature above its melting point. The bis-hydroperoxide of dichlorodiphenylanthracene has been prepared (370) in 70% yield by reaction with large excesses of hydrogen peroxide in the presence of pyridine as a chlorine acceptor.



The bis-hydroperoxide explodes when heated. An organic silicon peroxide has been formed (38) by the action of hydrogen peroxide on triphenylchlorosilane.

$$(C_6H_5)_3SiCl \longrightarrow (C_6H_5)_3Si\text{-}OO\text{-}Si(C_6H_5)_3$$

Di(triphenylsilyl) peroxide is a possible polymerization catalyst.

Typical Procedure – Preparation of Diacyl Peroxide (395)

Prepare a solution of sodium dihydrogen phosphate (15 g.) and disodium hydrogen phosphate (15 g.) in 400 ml. of water. Cool the solution to 5°C. by means of an ice-water bath, and add sodium peroxide (8 g.) with stirring. Maintaining the reaction temperature at 5°C., stir in a solution (cooled previously to 5°C.) of phthalyl chloride (14 ml.) in chloroform (300 ml.). Continue stirring for 15 minutes, separate the chloroform layer, and wash twice with water. Evaporate the chloroform solution at room temperature to about 30 ml. with a stream of air, and crystallize diphthalyl peroxide by cooling to -50°C. A 55% yield (8.9 g.) of crude peroxide is obtained after filtering off the crystals, washing with petroleum ether, and drying in a vacuum desiccator.

Organic Peroxides as Byproducts in Hydrogen Peroxide Reactions

The formation of organic peroxides has been presented from the standpoint of the reactivity of various functional groups to hydrogen peroxide. By considering these reactions, the chemist becomes aware of the possible formation of organic peroxides as byproducts in other reactions of hydrogen peroxide. If organic peroxides are byproducts every effort should be made to decompose residual peroxides with such ions, molecules, or agents which effect their destruction before undertaking such operations as distillation. Reducing agents and heavy metal ions are examples of such agents. Therefore, analytical procedures to detect organic peroxides in small quantities become very important.

The estimation (450) of organic peroxides is generally based on iodometric methods. The procedures usually involve the titration of iodine released by the oxidation of potassium iodide by an organic peroxide such as benzoyl peroxide.

$$(C_6H_5CO)_2O_2 + 2KI \longrightarrow 2C_6H_5COOK + I_2$$

Normal iodometric procedures are not successfully applied to all types of peroxides. The choice of solvent for such procedures appears to be very important and has included acetone, acetic acid, and isopropyl alcohol. A procedure for estimating benzoyl peroxide is given (435) by Swain. Hydroperoxides are usually determined (174) by the use of potassium iodide in isopropanol or glacial acetic acid. The method is not suitable for dialkyl peroxides. The method described as follows has been established (376) to estimate di-t-butyl peroxide and may be general for dialkyl peroxides:

Dissolve the sample in glacial acetic acid, and add an equal volume of constant boiling aqueous hydrogen iodide (about 56%) under an inert atmosphere. Close the container and heat the mixture at 60°C. for 45 minutes. Titrate the liberated iodine with standard thiosulfate solution after dilution with water.

The rates of oxidation of potassium iodide by various peroxide types are listed in the following order of probable decreasing rate: peracids, hydroperoxides, peresters, dialkyl peroxides, dimeric ketone peroxides, and trimeric ketone peroxides. This order has been established (408) on the basis of work done with sodium iodide in glacial acetic acid. Because of the decreased solubility of organic peroxides, aqueous medium is generally unsatisfactory for iodometric analyses of many peroxides. The lack of a suitable method for analyzing residual peroxides may require the evaporation of a small sample of the reaction mixture behind suitable barricades to determine whether or not a hazardous mixture is involved.

Reactions and Uses of Organic Peroxides

The reactions of the organic peroxides generally depend upon their decomposition into useful free radicals. Many of the reactions of organic peroxides, especially of diacyl peroxides and hydroperoxides, have been elucidated by Kharasch (262,

263). Since organic peroxides produce free radicals, they are used widely to initiate or catalyze free radical reactions. Such reactions include autoxidation, polymerization, telomerization (266), bromination (269), chlorination with sulfur chloride (260), halogenation with halogen gases (261), cis-trans isomerization (267), anti-Markownikoff addition to olefins (309), addition of phosphorus or silicon compounds to olefins and acetylenes (78), addition of alkoxy radicals to conjugated systems (259), and others. Hydroperoxides may also decompose to free radicals which combine (298) to form disubstituted peroxides. In the reactions enumerated above, the organic peroxides function as oxidants in abstracting electrons from donor molecules.

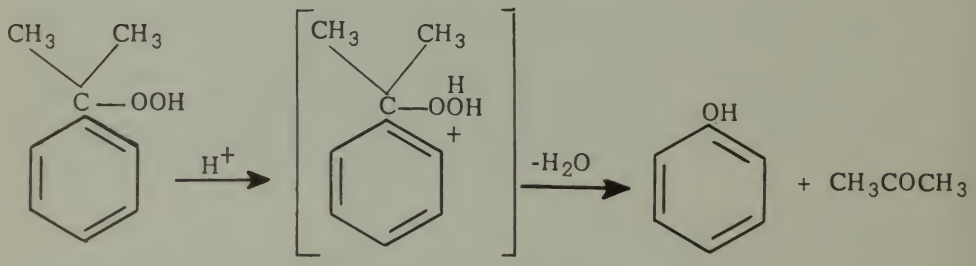
In many instances, organic peroxides donate (264) oxygen atoms to acceptor molecules and are oxidizing agents in the usual sense. Tetralin peroxide, for example, oxidizes (468) vanillin to vanillic acid although it is too mild to effect the cleavage of catechol to muconic acid. In other reactions, hydroperoxides are reduced (85) to alcohols, and hydroxy hydroperoxides under treatment with alkali form (220) the alkali salts of carboxylic acids. The reactions of the organic peroxides have been reviewed recently by Hey (78), Mesrobian and Tobolsky (450), and Hawkins (220).

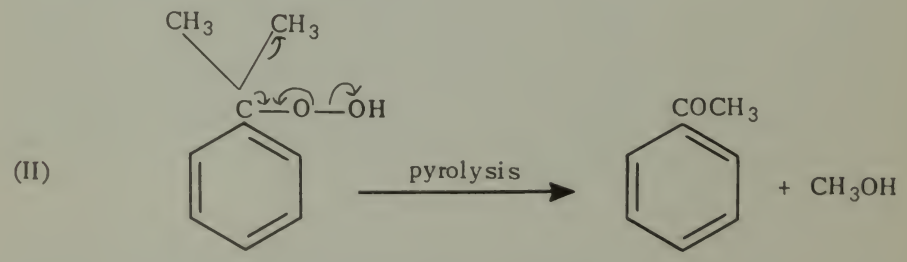
A growing commercial role for the organic peroxides involves their decomposition or rearrangement to useful products. Thus cumene is converted by air oxidation to cumene hydroperoxide, which is decomposed to give phenol and acetone. Since peroxides may be decomposed to useful products, a knowledge of the decomposition process (193, 450) is desirable.

The chemistry of the organic peroxides is easily understood if their decomposition (262) is assumed to be of three types: (1) an ionic decomposition under acid catalysis, (2) a free radical decomposition induced by heat or a reagent without the evolution of oxygen, and (3) a decomposition induced by heat or a reagent causing oxygen evolution. Alcohols are produced from hydroperoxides by a thermal decomposition or by the action of alkali or the reduced form of electromotive couples (240). A decomposition reaction carried out under acid catalysis at

elevated temperatures is complicated by a concomitant free radical decomposition. An exclusively ionic decomposition is obtained, however, by dissolving a hydroperoxide in glacial acetic acid and adding a small amount of perchloric acid. Lewis acids may also induce ionic decomposition if used in the proper solvents. A kinetic study of the thermal decomposition of benzoyl and other peroxides indicated (45) that the reaction is first order and independent of initial peroxide concentration.

The decomposition of cumene hydroperoxide offers an interesting study of the products obtainable by conscientious choice of reaction conditions favoring homolytic or ionic cleavage as desired. Cumene hydroperoxide produces (228) phenol and acetone under acid catalysis but probably forms (219) considerable acetophenone and methanol in a free radical-induced decomposition.





The acid-catalyzed reaction (I) probably involves the intermediate formation of an oxonium salt, which is stabilized by dehydration. The homolytic cleavage (II) of the peroxide to form acetophenone requires cleavage (a) of the peroxide bond followed by that (b) of the weakest C-C bond. Cleavage of the C-phenyl bond in cumene hydroperoxide would result in the formation of the relatively unstable phenyl

free radical. The methyl- and benzyl-derived free radicals, formed by the cleavage of the C-CH_3 bond are relatively stable. Therefore, it is assumed that C-CH_3 is the weaker bond and cleaves to form acetophenone. Cleavage of the C-phenyl bond would produce phenol and acetone in free radical-induced decomposition.

The uses for organic peroxides often depend upon their ability to produce reactive free radicals. Such organic peroxides as t-butyl perbenzoate and 2,2-di(t-butylperoxy)butane have been used (61) in rubber manufacture, producing gum vulcanizates with a high degree of transparency and good heat aging characteristics. Organic peroxides used with carbon black to process rubber reduce (142) the time required for low hysteresis processing. The higher molecular weight peroxides are (135) desirable additives for Diesel fuels, improving ignition properties as measured by cetane numbers. Conversely, however, they cause (383) the premature explosion ("knock") of fuel-air mixtures in gasoline engines. Peroxides are effective in catalyzing the drying of oils in coating applications and have also been used as depolymerization and bleaching agents. Organic peroxides are probably formed transiently in such biological oxidations as the conversion of ethyl alcohol to acetic acid in the presence of acetobacter. Organic peroxides have been used in bactericidal (280) and herbicidal compositions (204).

POLYMERIZATION

Vinyl Polymerization

Peroxides – including the organic peroxides, hydrogen peroxide, and such inorganic peroxides as sodium peroxide and potassium persulfate – are commonly used to induce the addition polymerization of vinyl compounds. Organic peroxides are believed to function by releasing free radicals which initiate polymerization.

$$RCO—OO—COR \longrightarrow 2RCO_2\bullet$$

$$2RCO_2\bullet \longrightarrow 2R\bullet + 2CO_2$$

The action of hydrogen peroxide in polymerization may depend upon its combining with the monomer or with a minor ingredient of the recipe to form an organic peroxide. It may also function by decomposing to an active hydroxyl free radical.

$$H_2O_2 + M^{++} \longrightarrow HO\bullet + M^{+++} + HO^-$$

The manner in which the persulfates induce polymerization is uncertain but is believed (282) to involve a sulfate free radical.

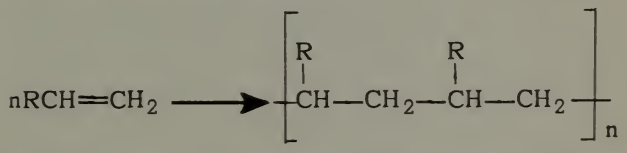
$$S_2O_8^{=} \longrightarrow 2SO_4^{-}\bullet$$

The peroxide initiators may be employed in a variety of techniques involving aqueous, emulsion, bulk, or solvent systems. Hydrogen peroxide is especially useful in aqueous and emulsion systems for polymerization.

Carothers has defined (173) polymerization as an intermolecular combination, functionally capable of proceeding indefinitely. Such intermolecular combination may involve a condensation, an association, or an addition reaction. Condensation polymerization occurs in the manner of ordinary organic reactions; that is, polymerizable molecules are combined by splitting off smaller molecules.

$$n HOOC(CH_2)_4COOH + n NH_2(CH_2)_6NH_2 \xrightarrow{-H_2O} \left[NHCO(CH_2)_4CONH(CH_2)_6NHCO\right]_n$$

Association polymerization usually is given a mysterious connotation but simply involves monomer or co-monomer units held together by semichemical bonds. Association polymerization may occur if the polymerizable materials possess such atoms as nitrogen, oxygen, or sulfur which offer association through hydrogen bonding. The stability of association polymers is much poorer than that of ordinary polymers because the semichemical bonds are easily dissociated. Addition polymers, in the sense of vinyl addition, are the products of the combination of unsaturated compounds.



Their manufacture represents an important use for hydrogen peroxide as a polymerization initiator and in the preformation of organic peroxides to be used to induce polymerization. Condensation and association polymerization do not ordinarily involve the use of hydrogen peroxide or related peroxides.

Olefins and substituted olefins are the usual subjects for addition polymerization reactions. The properties of olefins which make them polymerizable by hydrogen peroxide are not easily predicted. A terminal double bond was once considered necessary for polymerization. Terminal double bonds, however, are not required although their presence increases the tendency of the olefin to polymerize. The presence of electron-attracting groups adjacent to a double bond also promotes polymerization. Alkyl groups usually render polymerization more difficult although 2-methyl propylene is polymerized readily under the proper conditions. Certain vinyl monomers undergo copolymerization but are difficult to polymerize alone. Tetrafluoroethylene, by all rules, should resist polymerization. That tetrafluoroethylene polymerizes under certain conditions probably indicates that any olefin will polymerize if the proper conditions are established.

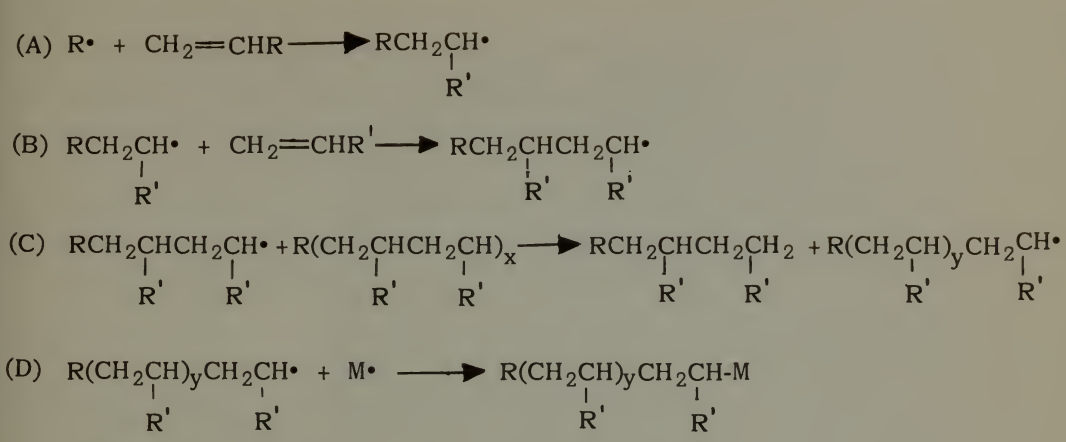
Unlike condensation polymerization, the mechanism of addition polymerization is complex. Addition polymerization was originally defined as the addition of unsaturated compounds to give integral multiple molecular weights of the original compounds. According to this definition, the polymer

had the same composition as the monomer. It was later shown that no polymer has the exact composition of its monomer because the process of polymerization usually involves side-chain reactions and is often ended by the addition of foreign molecules.

Side reactions generally involve solvents, diluents, modifiers, and small amounts of impurities which tend to decrease the molecular weight of the polymer. There is evidence also that the hydrogen peroxide or organic peroxide catalyst takes part in the side reactions under certain conditions. Polymerizations involving hydrogen peroxide are sensitive to such external conditions as pressure and temperature. Staudinger, who first insisted that polymers are organic materials, was also the first to point out that excess catalyst and excessive reaction temperatures decrease the polymer molecular weight by inducing side reactions.

Addition polymerization is rarely homogeneous. The molecular weights of addition polymers do not increase as the reaction proceeds as in condensation polymerization. In addition polymerization, the first fractions of the polymer formed have about the same magnitude of molecular weight as the last fractions. Few polymers are homogeneous in molecular weight although natural polymers are more so than synthetic polymers. Polymers with wide variations of molecular weights, as a rule, are not as useful as those with less variations. A reasonable distribution of molecular weights is desirable. The degree of homogeneity and the viscosity of the addition polymer often depend upon the stability of the peroxide catalyst under the conditions of its use in polymerization.

Addition polymerization is a chain reaction which involves free radicals when peroxide catalysts are used. Polymerization may also proceed by free radical and ionic mechanisms which do not require hydrogen peroxide or other peroxides as catalysts. The mechanism of addition polymerization must account for molecular weight distribution, polymer orientation, the nature of the end groups, and the prevalence of branching or cross-linking. The following mechanism which involves chain initiation (A), chain propagation (B), chain transfer (C), and chain termination (D) allows a satisfactory interpretation of the phenomena listed above:



Early mechanisms for addition polymerization included chain initiation, chain propagation, and chain termination steps. Flory (172) inserted a fourth step between the propagation and termination steps termed the chain transfer step (C) to account for the constancy of molecular weight in vinyl polymerization. Flory also postulated that two types of catalysts for vinyl polymerization existed: a positive catalyst accelerating step (A) and a negative catalyst accelerating step (D). Use of the negative catalyst inhibits polymerization, probably by a disproportionation rather than by a coupling process.

The chain branching step involves the reaction of a free radical, usually a propagated radical, and a complete polymer molecule. Exceptionally stable monomer or peroxide free radicals formed in the initiation process participate in the chain transfer step. In the presence of such stable free radicals, the tendency for branching increases. Excessive side chain branching destroys the symmetry of the polymer and alters such physical properties as crystallinity and viscosity. The use of hydrogen peroxide or other peroxides in polymerization, therefore, must be such that the free radicals which they generate are used effectively in the initiation step.

Marvel and co-workers have demonstrated (307) that hydrogen peroxide is not directly responsible for initiating the polymerization of butadiene and styrene. The presence of hydrogen peroxide is required, however, since polymerization fails in its absence. Hydrogen peroxide probably reacts with

one of the ingredients of the recipe to form an intermediate water-insoluble peroxide. The water-insoluble peroxide may be a soap peroxide formed in the emulsifier system since polymer conversion (four hours at 50°C.) varies considerably with the emulsifier used: standard soap flakes, 80%; potassium oleate, 67%; rosin soap and sodium alkylnaphthalenesulfonate, 6%. Kolthoff (281) has also shown soap peroxide to be the active agent in hydrogen peroxide recipes for GR-S polymerization.

Hydrogen peroxide is usually employed in emulsion techniques for polymerization although it may be used in bulk and solution polymerization also. Its effective use in bulk polymerization generally depends upon its solubility in a monomer with which it may react to form an intermediate organic peroxide. Bulk polymerizations are sensitive to variations in pressure, temperature, and catalyst concentration. Hydrogen peroxide has been used (9, 160, 161) in solutions to polymerize monomers which are solids or gases. The solvent allows easy removal of the final polymer from the reaction vessel. Drastic variations in polymer properties are also eliminated by better temperature control. The need for recovery of solvent, however, makes solution polymerization undesirable for many industrial applications. Hydrogen peroxide has never been used industrially in gas phase polymerization.

Emulsion polymerization is, therefore, the most important operative technique for hydrogen peroxide. Use of this technique permits ease of reaction control and a greater accessibility of the final polymer as a powder. The rate of emulsion polymerization is also generally greater than bulk or solution polymerization. However, bead polymerization often proceeds at a greater rate than emulsion polymerization.

The emulsion system consists of four major components: (a) water as the continuous phase, (b) the monomer(s), (c) the emulsifying agent, and (d) the catalyst. The emulsifying agent is usually a soap of saturated fatty acids, sulfonic acids, or invert soaps ($R_4N^+Cl^-$). Invert soaps, however, may form stable emulsions which are not easily broken in coagulating the polymer. The catalyst is usually hydrogen peroxide, organic peroxides, or potassium persulfate.

In the United States, an important development in polymerization techniques has been the use of modifiers as minor components of emulsion systems. Modifiers, often long chain mercaptans, are usually required in the manufacture of synthetic rubber to reduce stiffness by shortening the polymer molecule and to eliminate preheating of the polymer before milling. Other minor components of emulsion systems include promoters, stabilizers, surface tension regulators, and buffers. Such stabilizers as polyvinyl alcohol prevent premature coagulation of the polymer until an appreciable amount has been formed. Surface tension regulators are usually C_5-C_8 alcohols and are used to regulate particle size. Particle size is often affected by changes in pH; therefore, carbonates and phosphates are also used to regulate particle size. Promoters are simply the ferrous, titanous, cuprous, and manganous ions used in redox recipes to generate hydroxyl free radicals from hydrogen peroxide.

Hydrogen peroxide is often used in so-called redox recipes (9) to effect polymerization. Polymerization in such systems depends upon the use of catalysts like ferrous, titanous, manganous, and cuprous ion to effect a single electron transfer, activating hydrogen peroxide. The active species initiating polymerization may be the hydroxyl free radical.

(A) $H_2O_2 + Fe^{++} \longrightarrow {}^{\bullet}OH + Fe^{+++} + {}^{-}OH$

In the absence of monomer, the active free radical is probably destroyed by excess ferrous ion.

(B) $Fe^{++} + {}^{\bullet}OH \longrightarrow Fe^{+++} + {}^{-}OH$

The net result of reactions (A) and (B), in the absence of monomer, is the complete dissipation of hydrogen peroxide and the consumption of two moles of ferrous ion. In the presence of monomer, reaction (C) proceeds preferentially to induce polymerization.

(C) $RCH{=}CH_2 + {}^{\bullet}OH \longrightarrow RCHCH_2OH$

It should be pointed out, however, that the foregoing sequence of reactions is probably not a true representation of redox activation. The mechanism by

which polymerization is induced is undoubtedly much more complex. The sequence presented, nevertheless, offers a simple interpretation of the redox process.

The efficiency of polymerization is increased by conducting activation in combination with a suitable reductant. As pictured above, redox activation requires a mole of ferrous ion per mole of activated hydrogen peroxide produced and is not, therefore, a catalytic process. By using a suitable reductant to return ferric ion to the ferrous state, one may use much less ferrous or comparable ion as catalyst. The reductant is (281, 459) usually a reducing sugar or other oxidizable polyhydroxy compound such as glucose, levulose, sorbose, and invert sugars. The role of α-ketols (355) in reducing ferric ion is probably as follows:

$$\cdot OH + RCOCH_2OH \longrightarrow H_2O + RC\dot{O}CHOH$$

$$HO\dot{C}HCOR + Fe^{+++} \longrightarrow RC(O^-)=CHOH + Fe^{++}$$

The use of reducing agents with such oxidation catalysts as ferrous, manganous, cuprous, vanadous, and cobaltous ion allows a faster polymerization at much lower temperatures. As a result, such polymers as synthetic elastomers prepared by such systems have improved properties including those of strength and density.

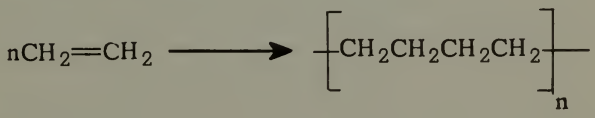
Other reductant-oxidant systems have also been used to advantage. An acyl hydrazide-copper salt initiator system containing hydrogen peroxide produced (237) a 93% conversion of methyl methacrylate to polymer at 25°C. Polymerization did not occur in the absence of the hydrazide. Dihexyl sodium sulfosuccinate used (291) with ferric ion and hydrogen peroxide effected the copolymerization of vinylidene and vinyl chloride at 22°C. Vinyl compounds have been polymerized by hydrogen peroxide under activation by the sodium formaldehyde sulfoxylate-Fe^{+++} system (41) and by zinc formaldehyde sulfoxylate (503). The reducing properties of arsenious

acid (As_2O_3) is used (495) to polymerize butadiene-styrene at extremely low temperatures (-18°C.). The rate of polymerization of acrylonitrile or styrene by hydrogen peroxide is accelerated (80) by conducting polymerization in the presence of hydroxylamine or its water-soluble salts. Other activators include the use (375) of polyethylene polyamine activators which help to reduce discoloration of polymeric articles caused by ferrous salts.

Polyamines have also been used (154) as effective reducers for hydroperoxide initiator systems. Uniform conversions of butadiene-styrene copolymers have been obtained by using a mixture of 80% diethyltriamine and 20% tetraethylene pentamine while adjusting polymerization rate by addition of ferrous iron. Similar amines are ineffective activators for butadiene-acrylonitrile. Apparently the polyamine activators are cyanoethylated resulting in a loss of reducing power.

Polyethylene

Polyethylene is one of the most difficult vinyl polymers (403) to manufacture and was, therefore, one of the last to be introduced commercially. The polymerization of ethylene is represented simply by the following equation:



The polymer molecule, however, does not have the simple linear structure indicated by the equation but is made complex by crosslinking and long- and short-chain branching. Crosslinking is usually undesirable because it restricts the fluidity of the product. Cathode-ray irradiation (100), however, crosslinks polyethylene to form useful insoluble, infusible plastics. Long- and short-chain branching – which affects such polymer properties as density, moisture permeability, hardness, and ultimate strength – can be controlled (99, 390) by careful manipulation of reaction conditions. The wide variety of reaction conditions under which polyethylene is formed allows the manufacture of such products as waxes, tough plastics, flexible and stiff polymers, and elastic melts.

Hydrogen peroxide is used to initiate polymerization of ethylene at low pressures but also to preform organic peroxide initiators for high pressure polymerization. The polyethylenes, which are generally wax-like products of low pressure processes using hydrogen peroxide, are manufactured at pressures ranging from 2000 to one atmospheres. Hard, high-melting waxes are obtained (160) by use of 0.1%-2% hydrogen peroxide in isopropanol at 425-475 atmospheres. Use of hydrogen peroxide concentrations out of this range tends to give softer waxes. Using hydrogen peroxide in a low molecular weight alcohol such as methanol produces (161) a mixture of C_5 to C_{25} saturated monohydric alcohols. The alcohols are valuable for the manufacture of plasticizers. Tertiary alcohols having average molecular weights of about 204 have been prepared (19) by condensing an alcohol, such as isopropanol, and ethylene in the presence of hydrogen peroxide. Conventional polyethylenes have been formed (235) at 1200 atmospheres by use of a polymerization initiator consisting of a mixture of ammonium persulfate and hydrogen peroxide. Generally speaking, low pressure polyethylenes are (104) of higher density because of less chain branching.

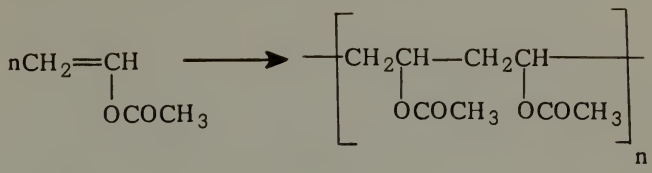
Polyethylenes are employed in the manufacture of films, moldings, and extrusion products. The polymer is inherently flexible and does not require the use of plasticizers. This is a fortunate property since the polyethylenes are not compatible with the conventional plasticizers.

Typical Procedure for the Polymerization of Ethylene (160)

Charge 10% of the volume of an 1820-cc. stainless steel autoclave with isopropanol. Add 0.4% hydrogen peroxide (as 30%) based on the weight of the isopropanol. Compress deoxygenated ethylene to 1000 atmospheres in a hydraulic compressor, and feed into the autoclave at 6200 p.s.i. Reaction begins at 150°C., the temperature varying up to 164°C. at pressures between 6800 and 7000 p.s.i. Continue reaction for 2.5 hours.

Polyvinyl Acetate

Hydrogen peroxide, properly activated in aqueous systems, brings about facile polymerization of vinyl acetate.

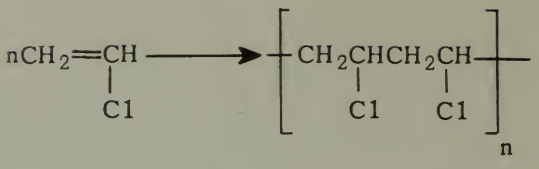


Among the activators used with hydrogen peroxide are zinc formaldehyde sulfoxylate (63), potassium ferrocyanide (84) and other iron salts (498), and ascorbic acid (503). A catalyst suitable for the polymerization of vinyl acetate has been prepared (182) by mixing equal amounts of aqueous hydrogen peroxide (30%) and vinyl acetate monomer, separating the aqueous and organic layers, and drying the vinyl acetate layer containing the peroxide. Low molecular weight polyvinyl acetate (341) and copolymers (136) with olefins such as ethylene have also been prepared with hydrogen peroxide. Vinyl acetate polymerization initiated with organic peroxides in bulk or solvent systems may be inhibited (73) with hydrogen peroxide. The principle is used to control the reaction or to stop polymerization when the polymer attains the desired molecular weight.

Water emulsions of polyvinyl acetate are useful (151) as adhesives, binders, coatings, paper and textile finishing agents, and vehicles for paints. Polyvinyl acetate emulsions have high mechanical and chemical stability and are easy to compound and apply. Films, coatings, and bonds are also produced from solutions or hot melts of polyvinyl acetate resins. Water-soluble polyvinyl alcohols — useful (148) as adhesives, binders, coatings, textile and paper sizing agents, and emulsifiers — are prepared from polyvinyl acetate by alkaline or acid-catalyzed hydrolysis.

Polyvinyl and Polyvinylidene Chlorides

Hydrogen peroxide has been used to polymerize vinyl and vinylidene chloride compounds.



In a continuous technique, emulsions containing vinyl chloride, aqueous sodium cetyl sulfate, and hydrogen peroxide are fed (134) continuously into each of a series of autoclaves at three atmospheres pressure (23°C.). Isobutene and vinyl or vinylidene chloride have been copolymerized (65) in a batch emulsion technique with a mixed hydrogen peroxide-ammonium persulfate catalyst. An activator system consisting of Cr^{+++} at low pH has also been used (69) with hydrogen peroxide to polymerize vinyl chloride in methanolic solution.

The polymers of vinyl and vinylidene chloride are important because of their insolubility in organic solvents. The polymers are plasticized to form rubber-like materials which are solvent-resistant, water-repellent, and suitable for electrical insulating materials and underwater cables. Polyvinyl and polyvinylidene chloride are colorless in their original form but become brittle and discolored under the action of sunlight. Such degradation, which is prevented by use of a fatty epoxy or other stabilizer, is due to loss of HC1 from the polymer chain. Vinyl plastics derived from these polymers are much used for sheeting, film, molding, and extrusion products.

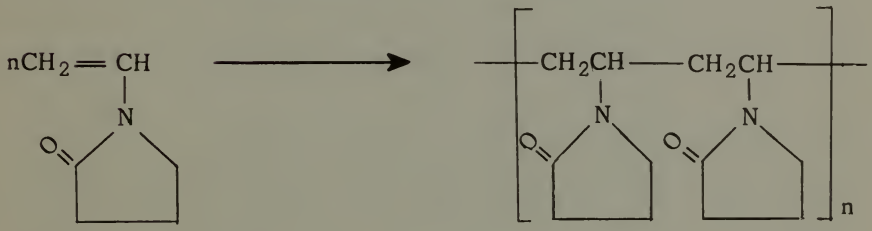
Miscellaneous Polymers

Many other vinyl polymers and copolymers have been prepared with hydrogen peroxide. In many cases, initiation of polymerization with hydrogen peroxide is dependent upon the formation of a hydroxyl free radical (162) or an intermediate organic peroxide. Butadiene-styrene polymers have been made (307, 357) by use of a metal-activated system which may involve the formation of an intermediate soap peroxide. Polymers of acrylonitrile and derivatives have been formed (123) by the photochemical dissociation of hydrogen peroxide in aqueous solution. A mixture of aged paraldehyde and hydrogen peroxide has effected (244, 306) the formation of polysulfones from

olefins and sulfur dioxide. Water-soluble polyacrylamide (81) and derivatives (139) are prepared by dissolving acrylamide in alcohol and heating the solution at 90°C. in the presence of hydrogen peroxide.

Peroxysilicas, capable of catalyzing the polymerization of unsaturates, are prepared (39) by adding finely divided silica to 90% hydrogen peroxide. Silica polymers are obtained by adding the dried peroxysilica product to polymerizable unsaturated materials.

N-vinyl lactam polymers are prepared (33) by polymerizing the monomer with repeated treatments of hydrogen peroxide made alkaline with ammonium hydroxide.



The usual techniques for polymerizing a N-vinyl lactam such as N-vinyl pyrrolidone, including treatment with aqueous sulfite solutions or organic peroxides, leave considerable unreacted monomer. N-vinyl lactam polymers, especially poly-N-vinyl pyrrolidone, are useful as blood plasma substitutes, drug extenders, and detoxifiers.

Typical Procedure for the Polymerization of N-Vinyl Pyrrolidone (33)

Charge reaction kettle with 160 lb. of N-vinyl pyrrolidone, 160 lb. of distilled water, 2178 ml. of 35% hydrogen peroxide, and 1452 ml. of 28% aqueous ammonium hydroxide. Heat the mixture for 11 hours at 50°C., and isolate the polymer by cooling. After spray drying, the product shows 3.08% residual unsaturation by analysis with 0.01N iodine solution.

Dissolve one pound of the above product in 6.6 lb. of distilled water, then add 18 ml. of 35% hydrogen peroxide and 18 ml. of 28% aqueous ammonium hydroxide. After immediate spray drying, the final product shows 1.1% unsaturation. An additional treatment with hydrogen peroxide and ammonium hydroxide reduces residual unsaturation to 0.65%.

HAZARDS OF HYDROGEN PEROXIDE

The oxidation of organic materials with hydrogen peroxide can usually be carried out in a controlled manner. Mixtures of organic substances and hydrogen peroxide, however, are sometimes explosive. Most of these mixtures are easily handled if the inherent hazards are recognized beforehand. The following paragraphs are written to help in the understanding of such hazards.

Hydrogen peroxide solutions obtained commercially are not explosive in the sense of a propagating detonation. If handled properly to avoid contamination, hydrogen peroxide may be stored indefinitely and transported from storage area to chemical operation with little difficulty. Gross contamination of peroxide solutions, however, may result in violent rupture of the containers with possible injury to personnel from flying metal or glass fragments. Proper handling of ordinary (35% to 50% concentrations) hydrogen peroxide solutions is achieved readily by teaching personnel concerned to abide by a few rudimentary principles of cleanliness and care. The ease with which such instruction is usually assimilated makes the occurrence of pressure ruptures in industry exceedingly rare.

High strength hydrogen peroxide solutions, containing over 52% by weight of H_2O_2 by definition, also present few hazards when properly handled. Such strengths as 90% hydrogen peroxide have not been detonated by impact or heat when not sensitized by contaminating organic or other materials. The explosion hazards of high strength hydrogen peroxide are almost always met during the course of its use. Such hazards are especially apparent in the use of high strength peroxide in organic oxidations. For this reason, the prospective user of high strength hydrogen peroxide should carefully assess whether a concentration such as 50% may not be equally satisfactory in his process.

Mixtures of hydrogen peroxide and organic substances may be explosive simply because organic peroxides have been formed in the mixture. Organic peroxides often exhibit high explosibilities. The term "explosibility" refers to the sensitivity of such compounds to detonation. Preformation of organic peroxides, however, need not necessarily occur to make organic mixtures of hydrogen peroxide

hazardous. Dangerous complexes of hydrogen peroxide and organic matter possibly are involved in certain mixtures. Other mixtures may be hazardous simply because the components have been mixed in the proper proportions in the absence of sufficient water. In any case, the possibility of prior formation of organic peroxides should be considered in any reaction involving hydrogen peroxide.

What Causes Explosions?

For explosive sensitivity, a material requires (a) an easily ruptured chemical bond releasing high energy and (b) favorable oxygen balance allowing the molecule to release energy in the formation of such small molecules as H_2O, CO_2, and CO. These small molecules are formed by the rupture and recombination of the atomic bonds of the explosive material (201, 299).

Condition (a) is met when the molecule contains two atoms of similar electronegativity joined together. In an explosive like TNT, oxygen and nitrogen are joined together in three nitro groups. These two atoms possess similar electronegativities and therefore form bonds which are ruptured with release of energy. In peroxides, two oxygen atoms are joined together. Having the same electronegativities, the two oxygen atoms form a bond (-O-O-) which is more easily ruptured than the -N-O bonds. Peroxides, therefore, meet condition (a).

An arbitrary rule may be used to estimate whether or not condition (b) applies. The rule states that molecules containing greater than 5% active oxygen should be judged hazardous. For example, the dangerous explosive, diacetyl peroxide (MW118), has a value in excess of 5% as calculated below:

$$\frac{16 \times 100}{118} = 13.5\%$$

Dibenzoyl peroxide, a much less sensitive peroxide, contains only 6.6% active oxygen. Therefore, dibenzoyl peroxide can be heated dry or refluxed in chloroform without exploding at temperatures below 95°C. Coumariloyl peroxide with 5% active oxygen has been exploded at 117°C. This last example appears to place an undue strain on the 5% rule. Lauroyl peroxide with 4% active oxygen has not been

exploded under ordinary conditions. The 5% rule appears to hold fairly well for such disubstituted peroxides as those mentioned above. The rule has less value, however, in comparing peroxides of dissimilar structure. Under the rule, peracids appear to be much more hazardous than diacyl peroxides. In many cases, the opposite may be true. Peracetic acid (21% active oxygen), for example, is more easily handled than diacetyl peroxide (13.5% active oxygen).

A good comparison of the sensitivities of peroxides with similar structures may be obtained by comparing their active oxygen contents. Performic acid (26% active oxygen) appears more hazardous than peracetic acid (21% active oxygen) in an analysis of this kind. That performic acid is more hazardous than peracetic acid under similar circumstances has been proved in practice (94).

The higher hydroperoxides such as t-butyl hydroperoxide are relatively harmless, at least in small quantities. Other peroxides with lower alkyl or acyl residues as well as di-, tri-, and polymeric ketone and aldehyde peroxides are extremely hazardous.

Some peroxides explode in the pure state even at very low temperatures. The ozonide (a type of peroxide) of maleic anhydride explodes at -40°C. This peroxide appears to hold the record for heat sensitivity. The peroxide of diphenylisobenzofuran explodes at 18°C.; acetaldehyde peroxide as soon as taken out of a cold mixture and placed on a watch glass.

Some peroxides show great sensitivity to friction. Ethyl hydroperoxide can be exploded by the sharp corners of its container. Methyl hydroperoxide cannot be obtained safely in quantities greater than 2 grams.

Peracetic acid solutions (69% or higher) can be exploded on impact. Pure peracetic acid explodes at 110°C. Performic acid (47% or greater) can be exploded by introducing contaminants of a catalytic nature.

Peroxides in exploding are brisant. Their explosions are characterized by a high shattering effect. In exploding, they generally exhibit detonation rates in the high explosive range – about 6000 meters/sec. They are, therefore, in the class with

TNT, tetryl, nitroglycerine, RDX and other high explosives. The explosive power of peroxides, however, is not used in military or industrial applications because peroxides are not normally considered stable enough for transportation and storage.

When Is Hydrogen Peroxide Explosive?

Whether or not pure hydrogen peroxide in the liquid state will explode appears to be questionable. There is definite evidence to suggest that a propagating detonation of the liquid is difficult to maintain. Recent studies (398, 399) indicate that hydrogen peroxide vapor can be exploded under appropriate conditions when the vapor concentration reaches 26 mole percent H_2O_2.

Many explosions reported for liquid hydrogen peroxide, therefore, may have occurred in the vapor phase. Hydrogen peroxide 94% has been exploded by boiling for a short period of time. Hydrogen peroxide 90% has not been exploded under conditions of impact and heat which have been reported so far. Boiling 98% hydrogen peroxide has been exploded (216) by passing the vapors through a pyrex tube containing a hot wire heated to 600°C. The explosions which resulted were extremely violent, resembling those of the dialkyl peroxides. Explosions of the vapor were obviously involved in the latter study.

The type of container employed may have considerable effect on the initiation of hydrogen peroxide explosions. Hydrogen peroxide of 99.6% strength could not be exploded (311) in thin-walled aluminum containers regardless of the primer employed. Explosions of this strength peroxide have occurred, however, in steel containers in the presence of a suitable detonator-primer combination. If sensitized with an organic material such as methanol, high strength hydrogen peroxide has been detonated in all containers tested.

Mixtures of high strength hydrogen peroxide and organic materials are, therefore, extremely hazardous. In general, mixtures with alcohols, ketones, and sugars are dangerous because of their insidious character. Such mixtures may give no indication of their extraordinary character but explode upon being moved. A mixture containing 67% hydrogen peroxide,

21% methanol, and about 12% water has been detonated, giving a detonation rate reported (311) as 6720 meters per second.

Ternary diagrams of systems containing organic material-hydrogen peroxide-water show (415) the explosibilities of such mixtures. The diagrams are amazingly similar for the organic materials studied. Typical systems are acetic acid-hydrogen peroxide-water and glycerine-hydrogen peroxide-water. From a study of these systems, it appears that a 10-ml. solution of an organic material containing 3 ml. of 90% hydrogen peroxide represents the lower limit of the explosibility range. The explosibilities of organic mixtures probably depend upon the type of organic compound involved and its mutual solubility with hydrogen peroxide. There is no reason, however, to preclude the possibility of explosions with dispersed or emulsified mixtures.

It is interesting to note what Criegee, the German peroxide chemist, writes about high strength hydrogen peroxide. The following is a translation from his review "Organic Peroxides" (118):

> "In the laboratory a high percent hydrogen peroxide is suitable for many of the reactions mentioned. In the U.S.A. a 90% product was prepared technically. There are detailed reports concerning its preparation and use. The stability is astonishingly good; with suitable storage the yearly decrease in content would amount to not more than 1%.
>
> "This product, although harmless in itself, requires extreme care in its use. Mixtures with organic compounds are high explosives, at least as good as nitroglycerine; in contrast to the latter they can detonate without apparent cause. One should, therefore, avoid the use of more than an 85% product and add not more than 5 cc. to 1 g. of material; even then all usual precautions should be taken. Note by the corrector: A recent extremely violent explosion in such an experiment makes it appear advisable to give up the use of excess high-percentage hydrogen peroxide completely, even when working on this small a scale."

Laboratory Precautions

The hazards involved in handling peroxygen compounds are those of fire, explosion, container ruptures, uncontrolled exothermic reactions, and damage to eyes or skin. As a general rule, contamination of peroxygen compounds should be carefully avoided. Spillage should be flushed immediately with large amounts of water. Many of the hazards presented by peroxides are common to the pyrophoric and corrosive chemicals familiar to all chemists. Precautions to avert such hazards, therefore, require little amplification in this section.

Exothermic reactions are also familiar to most chemists. Many reactions of hydrogen peroxide with large heat- or gas-release may proceed with explosive violence. The violence of these reactions is related to the inability of the surroundings to absorb the heat released or of the system to vent the gases produced. The following considerations taken from a Du Pont safety manual (397) apply to the potentially violent reactions of hydrogen peroxide:

1. "Unless the specific reaction is well known, the first runs should be on a very small scale."
2. "Any indication of an induction period, or delayed reaction, should be taken as a danger signal...." The addition of reagents should be halted until reaction begins. A good general rule to follow is to adjust addition of reagents to allow the temperature to rise to the prescribed range at a rate of about 2°/minute.
3. "All measures for reaction control should be simple, rugged, and sure to work. These control measures include gradual addition of reactants and effective stirring, heat dissipation, gas venting, and temperature indication. If possible, some means should be available for quenching the reaction in case of need."
4. "You and your neighbors should be protected by shielding. Personal protective equipment such as goggles and gloves should also be used in the vicinity of the experiment. Precautions should be taken against fire in case the reaction gets out of control."

For reactions of hydrogen peroxide which may be explosive or yield explosive products, the following considerations (397) apply:

1. "The scale of reaction should be limited to the smallest practicable quantity, in any case not more than one-tenth mol of potential explosive material. Micro-analytical techniques can help in drawing valid conclusions from this small-scale work."

2. "All personnel within the area should be completely shielded from direct line missiles. For the above scale, a minimum of 1/4" standard safety glass (not tempered glass), 1/4" 'Lucite' acrylic resin, or 1/16" mild steel is adequate. There should be a minimum spacing of ten inches between the shield and the reactor to prevent high-velocity fragmentation of the shield."

3. "All operations should be conducted by remote control."

4. Hydrogen peroxide should usually be added to the organic substrate or mixture containing the substrate. Addition of organic materials to the hydrogen peroxide may cause violent decomposition of the peroxide mass. Where explosive products are expected, an inert solvent should be used to dilute these products to a harmless concentration. The solvent should not be so volatile as to entrain explosive materials up the sides of the reaction flask to be deposited in concentrated form. The possibility of dangerous concentration of material by fractionation or separation of liquid phases should also be avoided.

5. "Cooling with dry ice or liquid nitrogen is helpful in manipulating explosive materials." Certain organic peroxides (93) explode, however, even when kept cold. The ozonide of maleic anhydride, for example, explodes at $-40^{\circ}C$.

6. If organic peroxides are possible byproducts of the reaction, the temperature of the bath used to heat the reaction mixture should not excede $100^{\circ}C$. If the reaction mixture is to

be distilled, every effort should be made to destroy residual peroxides prior to distillation. Decomposing agents which may be effective in many cases under the proper conditions include activated carbon, solutions of such metal salts as ferrous sulfate, lead chips, catalase, sulfur compounds with reducing properties, alkali, manganese dioxide, and other metallic compounds.

7. "Successful completion of small-scale experiments without explosion must never be taken to prove absence of hazard."

Little-known organic mixtures of hydrogen peroxide should be given detonation tests to determine their sensitivity to explosions. Such mixtures may be tested for heat sensitivity by putting a few drops on a clean, heated stainless steel plate. Stability toward explosion by impact may be tested by putting a few drops on a clean stainless steel plate and striking the drops with a hammer. Impact test machines, however, are available and should be used in lieu of the crude hammer test where possible.

Typical Fires and Explosions

Certain organic derivatives of hydrogen peroxide are extraordinarily sensitive to shock. Isolation of such compounds should be avoided if at all possible (119). Products of this type produced commercially are usually sold in diluted form or are of the less sensitive variety. Even so, unfortunate accidents in their use occur occasionally. The following are examples of typical fires and explosions reported by the National Board of Fire Underwriters (168):

"An explosion occurred on a tractor-trailer carrying about 300 pounds of benzoyl peroxide between two plants. The benzoyl peroxide was apparently exploded by shock when the trailer side-swiped another trailer going in the same direction. The peroxide which was packaged in 1-pound containers was compressed by the load of drums and other material behind it. All of the benzoyl peroxide was consumed in the explosion and there was no resultant fire. The load was scattered over the highway. Windows were blown out of a house nearby. The employees of the trucking concern were apparently not acquainted with the properties of the chemical.

"An operator in a polyvinyl acetate plant was killed when 12 pounds of dry benzoyl peroxide exploded as it was being added to a polymerization kettle. The benzoyl peroxide apparently exploded in the lower portion of a stainless steel funnel which had become heated during the operation. There was also the possibility that the benzoyl peroxide had become contaminated with residual vinyl acetate in the funnel. Tests conducted by this company indicated that such contamination increases the sensitivity of the chemical.

"An employee in a chemical laboratory was confronted with a flash fire when handling benzoyl peroxide. A glass spatula was being used to transfer small quantities of benzoyl peroxide from a 1-pound container to a laboratory scale. The spatula had been washed and dried before use. As it was inserted into the container, the peroxide flashed in a mass of flame. The employee sustained no serious injury, although, the lenses of his safety glasses were coated with melted benzoyl peroxide.

"A fire and explosion occurred on the premises of a small manufacturer of benzoyl peroxide. Cause of the fire was not discovered. The explosion which followed the fire ripped the structure apart and threw burning embers a distance of over 100 feet. A fire was started by these embers in the adjoining building which partially destroyed the roof.

"A fire took place on the premises of a benzoyl peroxide manufacturer. It was reported that this fire was started by the friction of a broom while the owner was sweeping benzoyl peroxide from the floor. The fire spread rapidly and soon involved benzoyl peroxide which was stored on the second floor of this building.

"A fire and explosion took place on the premises of this same benzoyl peroxide manufacturer. This fire was started by exposing benzoyl peroxide dust to an arcing electric light switch. The fire burnt fiercely, creating a considerable amount of smoke and chemical fumes before an explosion occurred. The owner of the plant was the only one in the building at this time and he managed to escape with second degree burns.

"Eleven men were killed and thirty-seven people were injured in an explosion that occurred during the manufacture of tertiary butyl peracetate. The two-story brick building used for this operation was totally destroyed and many houses nearby received varying degrees of structural damage. About 3000 pounds of the tertiary butyl peracetate, which was stored near the process equipment, was completely consumed in the explosion. A large crater was noticed in the location where this material was stored. All persons who could have related the exact sequence of events leading to the explosion were killed in the blast.

"Acetyl peroxide was being used in a chemical laboratory when it crystallized from a solution and exploded. About half of the prepared peroxide had been used in an experiment and the other half was placed in a small bottle and placed in a dry ice chest. A short time later a laboratory worker removed the acetyl peroxide from the chest and carried it back to the laboratory. It was reported that the 5 grams of acetyl peroxide in the bottle exploded with sufficient force to tear off both of the man's hands."

Conclusions

The above discussion on *The Hazards of Hydrogen Peroxide* is given to impress upon the chemist or worker that peroxides are not ordinary chemicals. The discussion is certainly not intended to induce fear of the peroxides nor to suggest that their use be restricted. It is hoped that the caution which is implied will help in the understanding of the chemistry of hydrogen peroxide and other peroxides and so encourage their increasing use.

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QD 281 O9W34
Wallace, John G.
Hydrogen peroxide in organic chemistry

c. bra n/a

3 4D3 015

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QD 281 O9W34
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